IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re Application of: James P. Elia)
)
Serial No.: 09/064,000)
)
Filed: April 21, 1998)
)
For: METHOD FOR GROWTH)
OF SOFT TISSUE)

Group Art Unit: 1646

Examiner: Elizabeth C. Kemmerer, Ph.D.

DECLARATION OF RICHARD HEUSER, M.D.

I Richard Heuser declare as follows:

1. I have offices at 525 North 18th Street, Suite 504, Phoenix, Arizona 85006.

2. My Curriculum Vitae ("CV") is attached hereto as Exhibit A.

3. In addition to my CV, I am currently Director of Cardiovascular Research at St. Joseph's Hospital and Medicine Center, and I serve as Clinical Professor of Medicine at University of Arizona College of Medicine. Over the past six years, I have worked in gene therapy, as well as muscle regeneration for the treatment of cardiomyopathy.

   In my CV, you will note reference to work that was done with Sulzer Medical involving a rabbit hind limb model to stimulate peripheral vascular disease. I injected a growth mixture that included FGF, etc. into the hind limb model.

In my U.S. Patent No. 6,190,379 entitled "Hot Tip Catheter," I developed a technique to deliver radiofrequency (PMR). In the full embodiment of the patent, I discuss delivery of protein and/or muscle cells in the myocardium using the inventive technique.

I have been involved as a member of the scientific advisory board with the world leader in cardiomyocyte regeneration, Bioheart, Miami Lakes, Florida. This company has been involved with laboratory and clinical trials using skeletal muscle cultured and modified. The sample is then delivered into the myocardium via a surgical or catheter approach.

4. I have read and understood the disclosures of the above-referenced patent application at page 20, line 10 through page 21, line 15; at page 37, lines 19-25; at page 44, line 19 through page 46, line 16; and at page 47, line 22 through page 48, line 15. A copy of such disclosures is attached hereto as Exhibit B.

5. I note that the disclosures referenced in above Paragraph 4 relate to using a growth factor for promoting the growth of soft tissue, and more specifically, to a method of using a cell, such as a stem cell, to grow soft tissue, such as an artery.

6. I am aware of and have considered the definition of *growth factor* in the specification of the above-referenced patent application at page 20, line 10 through page 21, line 15. Such definition is set forth in Exhibit C. Also included in Exhibit C is a definition from the medical dictionary, MEDLINE plus: Merriam-Webster Medical Dictionary, a service of the U.S. NATIONAL LIBRARY OF MEDICINE and the NATIONAL INSTITUTES OF HEALTH. I find that the dictionary definition is consistent with that contained at page 20, line 10 through page 21, line 15 of the above-referenced patent application. I believe that both definitions

are appropriate for use in the field of tissue growth and would be understood by one skilled in the medical arts. Accordingly, I am adopting and utilizing the definition contained in the patent application throughout this declaration.

7. I have read and understood the claims set forth in Exhibit D and have been informed that such claims are present in the above-referenced patent application. It is my opinion that those skilled in the medical arts, reading such claims would understand that cells including stem cells, are species of living organisms.

8. The publication in attached Exhibit E illustrates that placement of a growth factor, including cells, and more specifically, stem cells, in a human patient forms soft tissue, such as an artery. This publication reports work performed by reputable, skilled scientists and reputable organizations in the medical arts. Consequently, I believe that these reports would be recognized as clearly valid by one of ordinary skill in the medical arts because they report the results of scientific tests conducted by competent, disinterested third parties with use of proper scientific controls.

9. Based upon above Paragraphs 4-8, it is my opinion that introducing a growth factor, including cells, and more specifically, stem cells, in the body of a human patient will predictably result in the growth of soft tissue, such as an artery.

10. Based upon above Paragraphs 4-7, it is my opinion that one skilled in the medical arts, armed with the knowledge in such paragraphs, would be able to practice the method set forth in Exhibit D without need for resorting to undue experimentation.

11. Declarant states that the above opinion was reached independently.

Declarant understands that (1) any willful false statements and the like made herein are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of the application or any patent issuing thereon, and (2) that all statements made of Declarant's own knowledge are true and that all statements made on information and belief are believed to be true.

Further Declarant sayeth not.

Date: 11/11/04

Richard Heuser

Curriculum Vitae
Richard Ross Heuser, M.D., F.A.C.C., F.A.C.P.

ADDRESS:

525 North 18th Street, Suite 504
Phoenix, Arizona 85006
(602) 234-0004
(602) 234-0058 (fax)
phoenixheart@earthlink.net

EDUCATION:

1969 - 1972	University of Wisconsin Honors in Chemistry Phi Beta Kappa Evan Helfaer Scholarship in Chemistry
1972 - 1976	University of Wisconsin School of Medicine Graduation with Honors – May 1976 Alpha Omega Alpha Evan Helfaer Scholarship in Medicine

POST GRADUATE TRAINING:

1976 - 1977	Internship in Medicine The Johns Hopkins Hospital Baltimore, Maryland
1977 - 1979	Residency in Medicine The Johns Hopkins Hospital Baltimore, Maryland
1979 - 1981	Fellowship in Cardiology The Johns Hopkins Hospital Baltimore, Maryland

LICENSURE:

State of Arizona, License #19703
State of New Mexico, License #83-220

EMPLOYMENT:

December 2002 - Present	Director of Cardiovascular Research St. Joseph's Hospital and Medical Center Phoenix, Arizona
April 2001 - Present	Cardiac Cath Lab Director St. Luke's Medical Center, Phoenix, Arizona
June 2000 - Present	Medical Director Discovery Alliance, Phoenix, Arizona
1998 - June 2000	Director Phoenix Research Center, Phoenix, Arizona

April 1997 - Present	Medical Director Phoenix Heart Center, Phoenix, Arizona
December 1999 - Present	Director of Research St. Luke's Medical Center, Phoenix, Arizona
April 1997 - December 1999	Director of Research and Education Phoenix Regional Medical Center, Phoenix, Arizona
April 1990 - April 1997	Director of Research and Education Arizona Heart Institute, Phoenix, Arizona
July 1983 - April 1990	Private Practice New Mexico Heart Clinic, Albuquerque, New Mexico
July 1982 - June 1983	Private Practice Houston Cardiovascular Associates, Houston, Texas
June 1981 - July 1982	Instructor in Medicine, Cardiology The Johns Hopkins Hospital, Baltimore, Maryland

PROFESSIONAL APPOINTMENTS:

1981 - July 1982	Instructor in Medicine - Cardiology Division of Cardiology The Johns Hopkins Hospital, Baltimore, Maryland
July 1982 - June 1983	Instructor in Medicine, Cardiology Baylor College of Medicine, Houston, Texas
July 1983 - February 1990	Director, Interventional Cardiology New Mexico Heart Clinic, Albuquerque, New Mexico
April 1984 - June 1986	Clinical Assistant Professor of Medicine University of New Mexico, Albuquerque, New Mexico
	Director, Medical Residency Program New Mexico Heart Clinic, Albuquerque, New Mexico
June 1986 - April 1990	Clinical Associate Professor of Medicine University of New Mexico, Albuquerque, New Mexico
May 1996 - April 1997	Director, Interventional Cardiology Arizona Heart Institute Foundation, Phoenix, Arizona
Sept 1995 - December 1999	Medical Director - Cardiac Catheterization Laboratory Phoenix Regional Medical Center, Phoenix, Arizona
December 1990 - Present	Clinical Associate Professor of Medicine University of Louisville, Louisville, Kentucky
April 1990 - April 1997	Director of Research and Education Arizona Heart Institute Foundation, Phoenix, Arizona

April 1997 - December 1999 Director of Research and Education
Phoenix Regional Medical Center, Phoenix, Arizona

BOARD MEMBERSHIPS:

American Board of Internal Medicine
American Board of Cardiovascular Diseases, Diplomat
American Board of Interventional Cardiovascular Diseases, Diplomat

PROFESSIONAL MEMBERSHIPS:

Fellow, American College of Angiology
Fellow, American College of Cardiology
Fellow, American College of Physicians
Fellow, of the American Heart Association
Fellow, American Society of Cardiovascular Interventions
Fellow, International Society of Cardiovascular Interventions
Fellow, Society for Cardiac Angiography and Interventions
Member, American Association for the Advancement of Science
Member, American Heart Association
Member, American Medical Association
Member, Houston Cardiology Society
Member, Houston Society of Internal Medicine
Member, International Andreas Grüntzig Society
Member, International Network of Interventional Cardiology
Member, International Society for Carotid Artery Therapy
Member, International Society for Minimally Invasive Cardiac Surgery
Member, New Mexico Medical Society
Member, Harris County Medical Society
Member, Texas Medical Association
Member, National Register's Who's Who in Executives and Professionals
Member, Who's Who in Medicine and Healthcare 2002-2003

CLINICAL ADVISORY BOARDS:

Advanced Cardiovascular Systems
USCI
Mansfield Scientific Interventional Board
Medtronic Interventional Vascular
Scientific Advisory Board of International Society of Heart Failure

EDITORIAL BOARDS:

Catheterization and Cardiovascular Diagnosis
Journal of Endovascular Surgery
Cardiovascular Research Foundation/Society or Cardiac Angiography and Interventions
Abstract Grader TCT

DATA SAFETY BOARDS:

- ICEM Data Safety Monitoring Board

- Abbott Laboratories Data Safety Monitoring Board for Drug Coated Stent Program, PREFER, A Perspective STUDY to Evaluate the Safety and Efficacy of the ABT-578 coated BiodivYsio® Stent for the Reduction of Resetnosis

CONSULTANT TO:

Editors of the *Annals of Internal Medicine*
Editors of *Catheterization and Cardiovascular Diagnosis*
Editors of *Circulation*
Editors of the *Journal of Invasive Cardiology*
Editors of the *American Journal of Cardiology*
Editors of *Web M.D.*
Annual Scientific Session Program Committee of the American College of Cardiology
Annual Scientific Session Program Committee of the American College of Cardiology
Abstract Advisor for Angioplasty; Stents
Annual International Symposium of Transcatheter Cardiovascular Therapeutics
Abstract Grader

DEVICE RESEARCH:

Sub-Investigator ACS Multi-Link Stent Trial Principal Investigator - ACS RX
Principal Investigator ACT-One Trial Principal Investigator - Angio-Seal Trial
Principal Investigator Balloon Expandable Intraluminal Stent for Subtotally Occluded Iliac Arteries
Principal Investigator Bard® Memotherm Carotid Stent Study
Principal Investigator BARRICADE Trial - The Barrier Approach to Restenosis: Restrict Intima and Curtail Adverse Events (JOMED JOSTENT)
Principal Investigator BEST Trial
Principal Investigator BetaCath System Trial
Principal Investigator Boehringer Ingelheim Pharmaceutics Protocol Comparing Micardis and COZAAR
Principal Investigator CABERNET Clinical Trial - Carotid Artery Revascularization using the Boston Scientific EPI FiltreWire EX™ and the EndoTex™ NexStent™
Principal Investigator CADILLAC Trial
Principal Investigator CAPRICORN Trial
Principal Investigator CAPTIVE - Cardioshield Application Protects During Transluminal Intervention of Vein Grafts by Reducing Emboli
Principal Investigator CARDIOMETRICS
Principal Investigator Carotid Wallstent Trial
Principal Investigator CAVEAT II Trial
Principal Investigator Clinical Investigation of the Magnum Wire vs. Standard Guide Wires during Total Occlusion Angioplasty
Principal Investigator Cook GR II Trial
Principal Investigator CORDIS Nitinol Carotid Stent And Delivery System for the Treatment of Obstructive Carotid Artery Disease
Principal Investigator Cordis Carotid Randomized Sapphire
Principal Investigator Cordis Bilateral AAA Device & Delivery System
Principal Investigator (CATS) Safe-Steer™ Wire System Coronary Artery Total Occlusion Study
Principal Investigator CREDO Trial
Principal Investigator Novoste CUP Trial
Principal Investigator CVD Accucath Infusion Catheter
Principal Investigator Duett Closure Devise
Principal Investigator EndoSonics Cath scanner Oracle - PTCA Catheter

Principal Investigator EPI FilterWire EX™ System During Transluminal Intervention of Saphenous Vein Grafts
Principal Investigator Extra Stent
Principal Investigator GREAT - Guided Radio Frequency Energy Ablation of Total Occlusions Using the Safe Cross™ Radio Frequency Total Occlusion Crossing System
Principal Investigator GRIP - Guided Radio Frequency in Peripheral Total Occlusions using the Safe-Cross™ Radio Frequency (RF) Total Occlusion (TO) Crossing System
Principal Investigator HIPS Trial
Principal Investigator Human Percutaneous Laser Angioplasty of the Coronary Arteries
Principal Investigator Johnson & Johnson Intracoronary Stent Program Supplement #27 "New" Delivery System
Principal Investigator Kensey Nash Hemostatic Puncture Closure Device
Principal Investigator Mansfield-Boston Scientific Strecker Coronary Stent
Principal Investigator Medtronic AVE S7 with Discrete Technology Coronary Stent System
Principal Investigator Medtronic AVE S7 Coronary Stent Registry
Principal Investigator MOBILE Trial - More Patency with Beta for In-Stent Restenosis in the Lower Extremities Trial IDE #G010295; Protocol D00789 Rev B dated 12/01
Principal Investigator NIR Stent Trial
Principal Investigator Neurex/Elan Pharmaceuticals Trial
Principal Investigator PAMI Stent Trial
Principal Investigator Paragon Stent
Principal Investigator Paris Radiation Trial
Principal Investigator PaS Trial
Principal Investigator Percutaneous Coronary Angioscopy in Unstable Angina
Principal Investigator Percutaneous Recanalization of Stenotic Human Coronary Arteries with Balloon Expandable Intracoronary Stents
Principal Investigator Percutaneous Recanalization of Stenotic Human Saphenous Vein Bypass Graft with Balloon Expandable Intraluminal Stents
Principal Investigator Percutaneous Thermal Balloon Angioplasty
Principal Investigator PMR Trial
Principal Investigator Pravastatin or Atorvastatin Evaluation and Infection Therapy (Prove It)
Principal Investigator Presto Trial
Principal Investigator RAVES Trial
Principal Investigator RESCUE Trial
Principal Investigator SAFER - Saphenous Vein Graft Angioplasty Free of Emboli Randomized Study Using the PercuSurge Guard Wire™ System
Principal Investigator SAVED Trial
Principal Investigator Schering-Plough Phase III Study of SCH 58235 in addition to Pravastatin compared to placebo in subjects with primary hypercholesterolemia
Principal Investigator Long-Term, Open-Label, Safety and Tolerability Study of SCH 58235 in Addition to Pravastatin in Patients with Primary Hypercholesterolemia
Principal Investigator Schneider WINS Trial
Principal Investigator SCORES Trial
Principal Investigator Sepracor Study of Norastemizole in Cardiac Compromised Subjects
Principal Investigator SMART Trial (National PI)
Principal Investigator SMART: Post-Approval Study
Principal Investigator SNAPIST - A Phase 2, Safety Study of Systemic Nanoparticle Paclitaxel (ABI-007) For In-Stent Restenosis; IND #63,082
Principal Investigator SOAR - Renal Stent
Principal Investigator Efficacy and Safety Study of the Oral Direct Thrombin Inhibitor H 376/95 Compared with Dose-Adjusted Warfarin (Coumadin) in the Prevention of Stroke and Systemic Embolic Events in Patients with Atrial Fibrillation (SPORTIF V)
Principal Investigator STARS Trial
Principal Investigator START Trial (National PI)
Principal Investigator STRATUS Trial
Principal Investigator STRESS III Trial

Principal Investigator	SUMO Trial
Principal Investigator	(SWING) Sound Wave Inhibition of Neointimal Growth
Principal Investigator	Talent Endoluminal Graft (High Risk & Low Risk)
Principal Investigator	Talent Endoluminal Spring Stent-Graft System
Principal Investigator	Tenax-XR Coronary Stent System
Principal Investigator	TITAN Trial
Principal Investigator	Trimedyne Excimer Laser Assisted Percutaneous Coronary Angioplasty
Sub-Investigator	Trimdyne Percutaneous Eclipse Holmium Laser Coronary Angioplasty
Principal Investigator	VeGAS 2 Trial
Principal Investigator	Velocity Trial Principal Investigator - Venus Stent
Co-Investigator	WALLSTENT Study
Principal Investigator	WIKTOR Coronary Stent

PHARMACOLOGY RESEARCH:

Principal Investigator	Abbott rUK Trial
Principal Investigator	Ajinimoto Pharmaceuticals Double-Blind Placebo-Controlled Study of AT-1015 in Patients with Intermittent Claudication due to peripheral arterial disease
Sub-Investigator	Amgen, Inc. Anakinra Trial for Rheumatoid Arthritis
Principal Investigator	Astra Zeneca Pharmaceutical Trial to Evaluate the Safety and Efficacy of XXXX and Atorvastatin
Principal Investigator	Astra Zeneca Trial Open Label Dose Comparison Study to Evaluate the Safety and Efficacy of Rosuvastatin versus Atorvastatin, Pravastatin, and Simvastatin in Subjects with Hypercholesterolemia
Principal Investigator	Parke-Davis and Pfizer Randomized Open-Label Study Comparing the Efficacy of Once Daily Atorvastatin to Simvastatin in Hypercholesterolemic Patients
Principal Investigator	Pilot Study to Evaluate Intracoronary Administration of Activase for the Treatment of Intracoronary Thrombus
Principal Investigator	Artistic Trial
Principal Investigator	AstraZeneca Trial of Niaspan versus New Generation Statin for the Treatment of Type IIB and Type IV Hyperlipidemia
Principal Investigator	AstraZeneca Multicenter Trial for drug (XXX) and Atorvastatin for the Treatment of Hypercholesterolemia
Principal Investigator	BRAVO Trial
Principal Investigator	BioVail Angina & Hypertension Trial
Principal Investigator	CAPRICORN Trial
Principal Investigator	Challenge Trial
Sub-Investigator	Comparison of Lopentol and Omnipaque in Adult Angiocardiography
Sub-Investigator	Comparison of Intravenous Adenosine to Intravenous Placebo in Termination of Spontaneous or Induced Paroxysmal Supraventricular Tachycardia
Principal Investigator	Centocor Chimeric 7E3 Fab
Principal Investigator	COR Therapeutics Randomized Placebo-Controlled Dose Ranging Study of drug (XXXX) in Patients with Atherosclerotic Cardiovascular, Peripheral Vascular, and/or Cerebrovascular Disease
Sub-Investigator	Dose Response Study of Bucindolol in Patients with Congestive Heart Failure
Principal Investigator	Effects of Recombinant Human Superoxide Dismutase in Patients with Acute Myocardial Infarction Subject to Coronary Artery Reperfusion
Sub-Investigator	Eli Lilly - Agitation/Alzheimer's Trial
Principal Investigator	EPILOG Trial
Principal Investigator	ERASER Trial
Principal Investigator	GUSTO Trial
Principal Investigator	A multi-center, randomized, double blind, placebo-and-active controlled Parallel Group Dose-ranging Study of the HMG CoA Reductase Inhibitor, BMS-423526, in the treatment of Hyperlipidemia

Principal Investigator	Study Lovastatin XL with MEVACOR in patients with hypercholesterolemia
Sub-Investigator	Lovastatin Multi-Center Trial
Principal Investigator	Extended Trial of Lovastatin XL for the treatment of hypercholesterolemia
Principal Investigator	Multicenter Double-Blind Placebo controlled trial of drug (XXXX) in patients with Type 2 Diabetes and Congestive Heart Failure
Principal Investigator	Effect of LDL-Cholesterol Lowering Beyond Currently Recommended Minimum Targets on coronary heart disease (CHD) Recurrence in patients with Pre-Existing CHD
Principal Investigator	A Double-Blind, Multi-Center, Randomized, Placebo-Controlled, Parallel Group Dosing Study Evaluating the Effects of Nebivolol on Blood Pressure in Patients with Mild to moderate Hypertension, NEB 302
Principal Investigator	Parallel Group Extension Study to Determine the Safety and Efficacy of Long-Term Nebivolol Exposure in Patients with Mild to Moderate Hypertension NEB 306,
Sub-Investigator	NeoTherapeutics Alzheimer's Disease 2000
Sub-Investigator	NeoTherapeutics Alzheimer's Disease 2001
Principal Investigator	OCTAVE Trial
Sub-Investigator	OCTAVE Trial
Principal Investigator	Pfizer Phase II Multicenter, double-blind placebo controlled randomized parallel group dose ranging study of the safety of CP529,414 soft-gel capsules
Principal Investigator	PLAC Trial
Principal Investigator	Protocol 073 Trial
Principal Investigator	Knoll Pharmaceutical Double-Blind Randomized Clinical Trial of Slow Release Propafenone (Rythmol-SR®) in the Prevention of Symptomatic Recurrences of Atrial Fibrillation
Principal Investigator	PREVAIL - A Phase 2 Multicenter, Double-Blind Placebo-Controlled, Dose-Ranging Study to Evaluate the Safety and Efficacy of BO-653 in Prevention of Post-Angioplasty Restenosis in Stented Lesions
Principal Investigator	PROVE-IT TIMI 22 - Pravastatin or Atorvastatin Evaluation and Infection Therapy
Principal Investigator	PURSUIT Trial
Principal Investigator	QUIET Trial
Principal Investigator	RAFT Trial
Principal Investigator	REPLACE Randomized Evaluation in PCI Linking Angiomax to reduce Clinical Events
Sub-Investigator	Safety and Efficacy Study of Burroughs - Wellcome Tissue Plasminogen Activator in Patients with Acute Myocardial Infarction
Principal Investigator	A 6-week, open-label, dose-comparison study to evaluate the safety and Efficacy of Rosuvastatin versus Atorvastatin, Cerivastatin, pravastatin, and Simvastatin in subjects with hypercholesterolemia
Principal Investigator	A 48-week, open-label, non-comparative, Multicentre, Phase IIIb study to evaluate the efficacy and safety of the Lipid-Regulating agent Rosuvastatin in the treatment of subjects with Fredrickson Type IIa and Type IIb Dyslipidemia, including Heterozygous Familial Hypercholesterolemia
Principal Investigator	SAGE Trial
Sub Investigator	Long Term Open Label Safety and Tolerability Study of SCH58235 inn addition to Pravastatin in Patient With Primary Hypercholesterolemia
Principal Investigator	Phase III Double-Blind Efficacy and Safety Study SCH58235 (10 mg) in Addition to Pravastatin Compared to Placebo in Subjects with Primary Hypercholesterolemia
Principal Investigator	Phase III Open Label Efficacy and Safety Study SCH58235 (10 mg) in Addition to Pravastatin Compared to Placebo in Subjects with Primary Hypercholesterolemia
Principal Investigator	Sepracor Protocol Study of Norastemizole in Cardiac Compromised Subjects
Principal Investigator	SPORTIF V - Atrial Fibrillation Trial
Principal Investigator	SWORD Trial
Principal Investigator	Titration-to-Response Trial Comparing Micardis and COZAAR® in Patients with Mild-to-moderate Hypertension

Principal Investigator	TNT Trial
Principal Investigator	TREND Trial
Sub-Investigator	VALDECOXIB Trial
Principal Investigator	An Open-Label, Multinational, Multicentre, Extension Trial to Assess the Long-Term Safety and Efficacy of ZD4522 in Subjects in the ZD4522 Clinical Trial Program

BASIC RESEARCH:

1990 - 1993	Systematic assessment of Medtronic balloons and guiding catheters in porcine and canine models. Sponsored by Medtronic, Inc.
1990 - 1993	Determination of radiopacity and torquability of Medtronic vascular catheters in porcine models. Sponsored by Medtronic, Inc.
1992 - 1996	Evaluation of Strecker stent in porcine and canine models. Sponsored by Boston Scientific
	Evaluation of Wiktor stent and stent in porcine and canine models. Sponsored by Medtronic, Inc.
	Evaluation of NIR stent in porcine models. Sponsored by Cordis Corp.
1990 - 1994	Evaluation of Japan Crescent radiofrequency balloon in porcine model with emphasis on histopathology of heat-produced lesions. Abstract submitted at 1993 AHA Conference.
1993	Evaluation of radiofrequency wire for total coronary occlusions in porcine models: Determining energy limitations. Equipment subsequently licensed to Radius Medical.
1994 - 1997	Training courses for professionals (physicians, engineers, technicians) in techniques and strategies for placement of coronary stents. Five courses sponsored by Johnson & Johnson, Medtronic, Inc. and Cook, Inc.
1997	Efficacy of the Endotex Abdominal Aortic Aneurysm exclusion device in a porcine model gauging ability to exclude renal arteries, ease of placement and radiopacity. Sponsored by Endotex
1998	Use of percutaneous myocardial revascularization in a porcine model. Sponsored by Cardiogenesis Corporation at Stanford University.
1998 - 1999	Utility of radiofrequency (RF) percutaneous myocardial revascularization in acute and chronic porcine model: Histopathology and angiogenesis related to use of RF alone and in combination with growth factor (VEGF). Results presented at Angiogenesis 1999, Washington, DC.
1999	Development and testing of embolic probe device in porcine model (patent pending). Performed at PRMC and separately at Columbia Presbyterian in New York.
1999	Evaluation of the Medtronic carotid and SVG stent in porcine carotid and saphenous vein graft lesions assessing ease of use and 30-day outcome. Sponsored by Medtronic, Inc.
1999	Development and testing of Protector vascular embolic protection device in

porcine model at Mayo Clinic (device patent pending).

1999 Evaluation of ability of intramuscular growth factor to stimulate angiogenesis in rabbit hindlimb model at 30 and 60 days post-procedure. Sponsored by Sulzer Medical.

1999 Use of *Vesseal* device to close porcine peripheral artery tears (patent #6,159,197) Sponsored by Phoenix Heart Center.

PUBLICATIONS:

Bayless TM, **Heuser RR**: Fulminant Colitis. Johns Hopkins Medical Journal 1979 May;144(5): 168-172.

Heuser RR, Achuff SC, Brinker JA: Inadvertent division of an anomalous left anterior descending coronary artery during complete repair of tetralogy of fallot. American Heart Journal 1982 Mar;103(3):430-432.

Fuchs RM, **Heuser RR**, Yin FC, Brinker JA: Limitations of pulmonary wedge V-waves in diagnosing mitral regurgitation. The American Journal of Cardiology 1982 Mar;49(4): 849-854.

Fuchs RM, Brin KP, Brinker JA, Guzman PA, **Heuser RR**, Yin FC: Augmentation of regional coronary blood flow by intraaortic balloon counterpulsation in patients with unstable angina. Circulation 1983 Jul;68(1):117-123.

Alexander EL, Weiss JL, Firestein GS, **Heuser RR**, Leitl G, Wagner Jr HN, Brinker JA, Ciuffo AA, Becker LC: Reversible cold-induced abnormalities in myocardial perfusion and function in systemic sclerosis. Annals of Internal Medical 1986 Nov;105(5):661-668.

Heuser RR: Cardiogenic shock treated by PTCA. Cardiology 1987;4(6):64-66.

Heuser RR, Maddoux GL, Goss JE, Ramo BW, Raff GL, Shadoff N: Coronary angioplasty for acute mitral regurgitation due to myocardial infarction: A nonsurgical treatment preserving mitral valve integrity. Annals of Internal Medical 1987 Dec;107(6):852-855.

Maddoux GL, Goss JE, Ramo BW, Raff GL, **Heuser RR**, Shadoff N, Wilson JN, Deane WM, Hoyt TW, Fowler BN, Gerety RL, Hoffman AR: Left main coronary artery embolism: A case report. Catheterization and Cardiovascular Diagnosis 1987 Nov-Dec;13(6):394-397.

Maddoux GL, Ramo BW, Goss JE, Raff GL, **Heuser RR**, Shadoff N, Leatherman GF, Blake K, Wilson JN, Deane WM, Hoyt TW, Fowler BN, Gerety RL, Sansonetti E: Angina and vasospasm at rest in a patient with an anomalous left coronary system. Catheterization and Cardiovascular Diagnosis 1989 Feb;16(2):95-98.

Goss JE, Ramo BW, Raff GL, Maddoux GL, **Heuser RR**,, Shadoff N, Leatherman GF, Blake K: Power injection of contrast media during percutaneous transluminal coronary artery angioplasty. Catheterization and Cardiovascular Diagnosis 1989 Mar;16(3):195-198.

Heuser RR, Mehta SS: Holmium laser angioplasty after failed coronary balloon dilation: Use of a new solid-state, infrared laser system. Catheterization and Cardiovascular Diagnosis 1991 Jul;23(3):187-189.

Heuser RR, Mehta SS, Strumpf RK, Ponder R: Intracoronary stent implantation via the brachial approach: A technique to reduce vascular bleeding complications. Catheterization and Cardiovascular Diagnosis 1992 Apr;25(4):300-303.

Strumpf RK, Mehta SS, Ponder R, **Heuser RR**: Palmaz-Schatz stent implantation in stenosed saphenous vein grafts: Clinical and angiographic follow-up. American Heart Journal 1992 May;123(5):1329-1336.

Segal J, Kern MJ, Scott NA, King SB, Doucette JW, **Heuser RR**, Ofili E, Siegel R: Alterations of phasic coronary artery flow velocity in humans during percutaneous coronary angioplasty. The Journal of the American College of Cardiology 1992 Aug;20(2):276-286.

Heuser RR: The use of the Holmium: YAG laser in coronary disease: The utility of a unique lensed fiber catheter. The Journal of Interventional Cardiology 1992 Dec;5(4):293-300.

Heuser RR, Eagan JT, Strumpf RK: Angioscopy in coronary interventions. Cardiology Intervention 1992;2(4):23-28.

Santiago O, Diethrich EB, **Heuser RR**, Gustafson G: What is the next step for the application of the Palmaz stent – the abdominal aorta? Angiology 1992;42:267-268.

Heuser RR, Mehta SS, Strumpf RK: The ACS RX™ flow support catheter as a temporary stent for dissection or occlusion during balloon angioplasty: initial experience. Catheterization and Cardiovascular Diagnosis 1992 Sept;27(1):66-74.

Diethrich EB, Santiago O, Gustafson G, **Heuser RR**: Preliminary observations on the use of the Palmaz stent in the distal portion of the abdominal aorta. American Heart Journal 1993 Feb;125(2):490-501.

Heuser RR: Lasers in coronary disease (commentary). Catheterization and Cardiovascular Interventions 1993;28:17.

Eagan JT, Strumpf RK, **Heuser RR**: New treatment approach for chronic total occlusions of saphenous vein grafts: Thrombolysis and intravascular stents. Catheterization and Cardiovascular Diagnosis 1993 May;29(1):62-69.

Heuser RR, Strumpf RK, Diethrich EB, Eagan JT, Hardigan KR: Intraluminal diagnostics, the "guide" to the future. Angiology 1993;44:6.

Heuser RR, Strumpf RK, Eagan JT, Hardigan KR: Experience with four types of coronary stents. Angiology 1993;44:6-7.

Heuser RR: The use of a new wire in a 6-year-old coronary artery occlusion: The Jagwire™ recanalization guidewire. Catheterization and Cardiovascular Diagnosis 1993 Jun;29(2): 173-176.

Heuser RR, Strumpf RK, Hardigan K: Use of the Doppler guidewire for intraluminal diagnosis to facilitate coronary intervention. American Heart Journal 1993 July; 126(1):213-218.

Strumpf RK, **Heuser RR**, Eagan Jr JT: Angioscopy: A valuable tool in the deployment and evaluation of intracoronary stents. American Heart Journal 1993 Nov;126(5):1204-1210.

Heuser RR: Current status of coronary stents: Promises and disappointments. Critical Issues 1993;2:1-13.

White CJ, Ramee SR, Collins TJ, Escobar AE, Karsan A, Shaw D, Jain SP, Bass TA, **Heuser RR**, Teirstein PS, Bonan R, Walter PD, Smalling RW: Coronary thrombi increase PTCA risk: Angioscopy as a clinical tool. Circulation 1996 Jan;93(2):253-258.

Fischman DL, Leon MB, Baim D, Schatz RA, Penn I, Detre K, Savage MP, Veltri L, Ricci D, Nobuyoshi M, Cleman M, **Heuser RR**, Almond D, Teirstein P, Fish D, Colombo A, Brinker J, Moses J, Hirshfeld J, Bailey S, Ellis S, Rake R, Goldberg S: For the STRESS Trial Investigators: A randomized comparison of coronary stent placement and balloon angioplasty in the treatment of coronary artery disease. The New England Journal of Medicine 1994; 331:396-501.

Aker UT, Kensey KR, **Heuser RR**, Sandza JG, Kussmaul III WG: Immediate arterial homostasis after cardiac catheterization: Initial experience with a new puncture closure device. Catheterization and Cardiovascular Diagnosis 1994 Mar;31(3):228-232.

Flaherty JT, Pitt B, Gruber JW, Topol E, **Heuser RR**, Rothbaum DA, Burwell LR, George BS, Kereiakes DJ, Deitchman D, Gustafson N, Brinker JA, Becker LC, Mancini CBJ, Weisfeldt ML, Werns SW: Recombinant human superoxide dismutase (h-SOD) fails to improve recovery of ventricular function in patients undergoing coronary angioplasty for acute myocardial infarction. Circulation 1994 May;89(5):1982-1991.

Fenton SH, Fischman DL, Savage MP, Schatz RA, Leon MB, Baim DS, King SB, **Heuser RR**, Curry C, Rake RC, Goldberg S: Long-term angiographic and clinical outcome after implantation of balloon-expandable stents in aortocoronary saphenous vein grafts. The Journal of the American College of Cardiology 1994; Dec 15;74(12):1187-1191.

Heuser RR: Breaking the barrier: Stenting in acute myocardial infarction (commentary). Catheterization and Cardiovascular and Diagnosis 1994;33:46.

Heuser RR: A wire in every lesion (commentary). Catheterization and Cardiovascular Interventions 1994;33:197.

Heuser RR: All the glitters in not gold (commentary). Catheterization and Cardiovascular Interventions 1994 Dec;33(4):330.

Savage MP, Fischman DL, Schatz RA, Teirstein PS, Leon MB, Baim DS, Ellis SG, Topor EJ, Hirschfeld JW, Cleman MW, Buchbinder M, Bailey S, **Heuser RR**, Walker CM, Curry RC Jr, Gebhardt S, Rake R, Goldberg S: For the Palmaz-Schatz Study Group: Long-term angiographic and clinical outcome after implantation of a balloon-expandable stent in native coronary circulation. The Journal of the American College of Cardiology 1994;24:1207-1212.

Heuser RR, Diethrich EB, Papazoglou C, Reynolds GT: Endoluminal grafting for percutaneous aneurysm exclusion in an aortocoronary saphenous vein graft: the first clinical experience. Journal of Endovascular Surgery 1995 Feb;2(1):81-88.

Diethrich EB, **Heuser RR**, Tarlian H, Eckert J, Cardenas JR,: Endovascular techniques in adult aortic coarctation: the use of stents for native and recurrent coarctation repair. Journal of Endovascular Surgery 1995 May;(2)2:183-188.

Aguirre FV, Topol EJ, Ferguson JJ, Anderson K, Blankenship JC, **Heuser RR**, Sigmon K, Taylor M, Gottlieb R, Hanovich G, Rosenberg M, Donohue TJ, Weisman H, Califf RM for the EPIC Investigators: Bleeding complications with the chimeric antibody to platelet glycoprotein IIb/IIIa integrin in patients undergoing percutaneous coronary intervention. Circulation 1995; June 15;91(12):2882-2890.

Heuser RR: Treatment alternatives for chronically occluded saphenous vein grafts. The Journal of Invasive Cardiology 1995 May;7(4):94-96.

Kussmaul III WG, Buchbinder M, Whitlow PL, Aker UT, **Heuser RR**, King SB, Kent KM, Leon MB, Kolansky DM, Sandza JG: Rapid arterial homeostasis and decreased access site complications after cardiac catheterization and angioplasty: Results of a randomized trial of a novel hemostatic device. The Journal of the American College of Cardiology 1995 June;25(7):1685-1692.

Wong SC, Baim DS, Schatz RA, Teirstein PS, King SB 3rd, Curry RC Jr, **Heuser RR**, Ellis SG, Cleman MW, Overlie P, etal. Immediate results and late outcomes after stent implantation in saphenous vs lesions: the multicenter US Palmaz-Schatz stent experience. The Palmaz-Schatz Study Group. Journal of the American College of Cardiology 1995 Sept;26(3):704-712.

Cardenas JR, Strumpf RK, **Heuser RR**: Rotational artherectomy in restenotic lesions at the distal saphenous vein graft anastomosis. Catheterization and Cardiovascular Interventions 1995 Sept;36(1):53-57.

Cohen DJ, Krumholz HM, Williams C, Baim DS, Brinker J, Cabin HS, **Heuser RR**, Leon MB, Moses J, Savage MP, Cleman M: In-hospital and one-year economic outcomes after coronary stenting or balloon angioplasty. Results from a randomized clinical trial. The Stent Restenosis Study Investigators. Circulation 1995 Nov.;1;92(9):2480-2487.

Heuser RR: A new breed of drug pusher? (commentary). Catheterization and Cardiovascular Interventions 1995;34:271.

Heuser RR: Recanalization of occluded SVGs: Is there light at the end of the graft? (commentary). Catheterization and Cardiovascular Diagnosis 1995 Dec;36(4):333-334.

Heuser RR: Percutaneous revascularization using endoluminal prostheses: Coming of age (commentary). Catheterization and Cardiovascular Diagnosis 1996 Feb;37(2):213-214.

Kussmaul WG, Buchbinder M, Whitlow PL, Aker UT, **Heuser RR**, King SB, Kent KM, Leon MB, Kolansky DM, Sandza JG: Femoral artery hemostasis using an implantable device (AngioSeal™) after coronary angioplasty. Catheterization and Cardiovascular Diagnosis 1996 Apr;37(4):362-365.

Heuser RR: Stents in jackets: The latest in endovascular haute couture. Catheterization and Cardiovascular Diagnosis 1996 Jun;38(2):179.

Heuser RR: "Homemade" stents: Penny-wise or pound-foolish? (commentary) Catheterization and Cardiovascular Diagnosis 1996 Oct;39(2):197.

Schultz RD, **Heuser RR**, Hatler C, Frey D: Use of c7E3 Fab in conjunction with primary coronary stenting for acute myocardial infarctions complicated by cardiogenic shock. Catheterization and Cardiovascular Diagnosis 1996 Oct;39(2):143-148.

Heuser RR: The Multi-Link stent: Another good idea. (commentary) Catheterization and Cardiovascular Diagnosis 1996 Dec;39(4):420.

Kussmaul WG, Sandza JG, Kolansky DM, Leon MB, Kent KM, King SB, **Heuser RR**, Aker UT, Whitlow PL, Buchbinder M: Femoral artery hemostasis using an implantable device (Angio-Seal™) after coronary angioplasty. Catheterization and Cardiovascular Interventions 1996;37:362-365.

Heuser RR, Hartz RS: Embolization of IMA side branch for post-CABG Ischemia. Ann Thorac Surgery 1997 Jun;63(6):1765-1766.

Heuser RR: Unlimiting our resources. (commentary) Catheterization and Cardiovascular Diagnosis 1997 Aug;41(4):415.

Krumholz HM, Cohen DJ, Williams C, Baim DS, Brinker J, Cabin HS, **Heuser RR**, Hirschfeld J, Leon MB, Moses J, Savage MP, Cleman M: Health after coronary stenting or balloon angioplasty: Results from the Stent Restenosis Study (STRESS). The American Heart Journal 1997 Sept;134(3):337-44.

Heuser RR: A Freudian stent? (commentary) Catheterization and Cardiovascular Interventions 1997;41:4.

Savage MP, Douglas JS, Fischman DL, Pepine CJ, King III SB, Werner JA, Bailey SR, Overlie PA, Fenton SH, Brinker JA, Leon MB, Goldberg S, **Heuser RR**: Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. The New England Journal of Medicine 1997;337:740-747.

Heuser RR, Lopez AN: Stenting, angioplasty and adjunctive treatments in acute myocardial infarction. Cardiology Rounds 1998;15:9:8-14.

Savage MP, Douglas Jr JS, Fischman DL, Pepine CJ, King SB, Werner JA, Bailey SR, Overlie PA, Fenton SH, Brinker JA, Leon MB, **Heuser RR**, Smalling R, Safian RD, Cleman M, Buchbinder M, Rake RC, Gebhardt S, Goldberg S for the Stent Restenosis Study (STRESS) Investigators: Efficacy of coronary stenting versus balloon angioplasty in small coronary arteries. The Journal of the American College of Cardiology 1998;31:307-311.

Heuser RR: Outpatient coronary angiography: Indications, safety, and complication rates. Herz 1998 Feb;23(1)21-26.

Heuser RR: Garbage in, garbage out. (commentary) Catheterization and Cardiovascular Interventions 1998 Apr;43(4):402.

Heuser RR: Success with carotid stenting: A stroke of good luck or the wave of the future? (commentary) Catheterization and Cardiovascular Interventions 1998 May;44(1)7-8.

Heuser RR: Stentus Noninterruptus. (commentary) Catheterization and Cardiovascular Interventions 1998;43:253.

Woodfield SL, Lopez AN, **Heuser RR**: Fracture of Coronary Guidewire During Rotational Artherectomy with Coronary Perforation and Tamponade. Catheterization and Cardiovascular Diagnosis 1998 Jun;44(2)220-223.

Heuser RR, Lopez AN: Stenting, Angioplasty, and Adjunctive Treatments in Acute Myocardial Infarction. Cardiology Review 1998;15:8-14.

Heuser RR: Endovascular Haute Couture Revisited: Ready-to-Wear Comes of Age. (commentary) Catheterization and Cardiovascular Interventions 1998 Nov;45(3):314.

Heuser RR: The Cure for a Rainy Day. (commentary) Catheterization and Cardiovascular Diagnosis Dec 1998;45(4):421.

Heuser RR, Lopez A: Abdominal Aorta Aneurysm and ELG: A Review of a Treatment in Its Infancy. Journal of Interventional Cardiology 1998 December (II);6:591-602.

Heuser RR, Woodfield SL, Lopez AN: Obliteration of a Coronary Artery Aneurysm with a PTFE-Covered Stent: Endoluminal Graft for Coronary Disease Revisited. Catheterization and Cardiovascular Interventions 1999 Jan;46(1):113-116.

Heuser RR: The Right Place, the Right Time. Catheterization and Cardiovascular Interventions 1999 Apr;46(4)450-451.

Heuser RR: The growing role of stents in coronary artery disease. Patient Care May 1999: 43-58.

Teirstein PS, Mann III JT, Cundey PE, Schechter E, Jacobs WC, Grines CL, Stagaman DJ, Lansky AJ, Hultquist MA, Kusnick BA, **Heuser RR**, Kleinert HD, Popma J: Low versus high-dose recombinant Urokinase for the treatment of chronic saphenous vein graft occlusion. The American Journal of Cardiology 1999 June 15;83(12) 1623-1628.

Heuser RR: Warming up to the reptilian heart (commentary). Catheterization and Cardiovascular Interventions 1999 Jul;47(3):360.

Heuser RR: Of Baling Wire and Bubble Gum. Catheterization and Cardiovascular Interventions 1999 August;47(4):495.

Heuser RR: Innovative Interventions. Catheterization and Cardiovascular Interventions 1999 Sept;48(1):113.

Cordero-Yordan H, Lopez AN., **Heuser RR:** Saphenous Vein Graft Intervention, The Journal of Interventional Cardiology 1999;12(6):495-497.

Cordero-Yordan H., Lopez AN, **Heuser RR:** Carotid Artery Percutaneous Transluminal Angioplasty and Stenting; The Journal of Interventional Cardiology 1999;12:499-504.

Heuser RR, Cordero-Yordan H: Carotid Artery Percutaneous Transluminal Angioplasty and Stenting: Indications, Technical Approach, and Complications. The Journal of Interventional Cardiology. 1999;12(6): 499-504.

Heuser RR: At Arms' Length: Should We Teach Radial and Brachial Access Techniques? Catheterization and Cardiovascular Interventions 2000 Jan;49(1):38.

Heuser RR: Coronary Lesions: The Good, the Bad, and the Ugly, Catheterization and Cardiovascular Interventions 2000 Jan;49(1):112.

Oesterle SN, Sanborn TA, Ali N, Resar J, Ramee SR, **Heuser RR**, Dean L, Knopf W, Schofield P, Schaer GL, Reeder G, Masden R, Yeung AC, Burkhoff D: Percutaneous transmyocardial laser revascularization for severe angina: the PACIFIC randomized trial. The Lancet (356) November 28, 2000;1705-1710.

Heuser RR, Houser F., Culler SD., Becker ER, Battaglia SL, Tarkington L, Simon AW: A Retrospective Study of 6,671 Patients comparing Coronary Stenting and Balloon Angioplasty; The Journal of Invasive Cardiology 2000;July 2000.

Heuser RR: Delivery Systems for Endoluminal Grafting of Abdominal Aortic Aneurysms: A Square Peg for a Round Hole? (commentary). Catheterization and Cardiovascular Interventions 2000 Jul;50(3):361.

Heuser RR, Cordero H, Gupta N, Underwood PL, Gogte ST: Intracoronary Autologous Blood to Seal a Coronary Perforation; Herz 2001; March 26;(2):157-160.

Heuser RR, Lopez A, Kuntz R, Reduto L, Badger R, Coleman P, Whitlow P, Iannone LA, Safian R, Yeung A, Moses J: SMART: The MicroStent's Ability to Limit Restenosis Trial. Catheterization and Cardiovascular Interventions 52:269-277 2001

Cordero H, Warburton KD, Underwood PL, **Heuser RR:** Initial Experience and Safety in the Treatment of Chronic Total Occlusions with Fiberoptic Guidance Technology: Optical Coherent Reflectometry. Catheterization and Cardiovascular Interventions Oct 2001; 54(2):180-187.

Heuser RR: If It Can Keep Eggs Off the Frying Pan... (commentary) Catheterization and Cardiovascular Interventions May, 2001; 53:5.

Heuser RR, Cordero H, Schroeder W, Weirick BA, Hatler CW, Underwood PL: Fiberoptic Guidance System for Treatment of Chronic Total Occlusions: Single Center Experience. Journal of the American College of Cardiology; February 2001 (37) Supplement A: 1158-38.

Heuser RR, Morales PA: Across the Great Divide (commentary) Catheterization and Cardiovascular Interventions. October 2001; 54(2):264.

Ellis SG, Mooney M, Talley DJ, Silber S, Teirstein PS, Rodriguez AR, Sanborn TA, FeldmanT, Leon M, Collins TJ, Wilentz JR, Saucedo JF, Leimgruber PP, Pichard A, Cohen DJ, Ramee SR, **Heuser RR,** Smalling RW, Kuntz RE, Gershony G: Assessment of the Safety and Efficacy of the Duett ™ Vascular Hemostasis Device - Final Results of the Seal Trial. American Heart Journal April 2002; 143(4):612-9.

Morales PA, **Heuser RR**: Chronic Total Occlusions: Experience with Fiber-Optic Guidance Technology - Optical Coherence Reflectometry. Journal of Interventional Cardiology; December 2001; 14:6:611-616.

Morales PA, **Heuser RR**: Peripheral Vascular Disease: Perspectives on Aortoiliac, Renal, and Femoral Treatments Using Catheter-Based Techniques. Journal of Interventional Cardiology; December 2001; 14:6:629-637.

Heuser RR, Laskey W, Lansky A, Popma J, Bonan R: Beta Radiation in Lesions>15 mm: A START Subgroup. Journal of the American College of Cardiology. (In Press)

Philip A. Morales, M.D., **RR Heuser**, Embolic Protection Devices. Journal of Interventional Cardiology; December 2002; 15:485-490.

Philip A. Morales, M.D., and **RR Heuser**, Guiding Catheter Aspiration to Prevent Embolic Events During Saphenous Vein Graft Intervention. Journal of Interventional Cardiology; December 2002; 15:491-498.

Jeffrey J. Popma, Mohan Suntharalingam, Alexandra J. Lansky, **Richard R. Heuser** , Burton Speiser, Paul S. Teirstein, Vincent Massullo, Theodore Bass, Randall Henderson, Sigmund Silber, Peter von Rottkay, Raoul Bonan, Kalon K.L. Ho, Alison Osattin, MPH; Richard E. Kuntz, for the Stents And Radiation Therapy (START) Investigators, Randomized Trial of 90 SR/90 Y B-Radiation Versus Placebo Control for Treatment of In-Stent Restenosis. Circulation; August 2002; 106:1090-1096.

EDITED TEXTBOOKS:

Heuser RR: *Peripheral Vascular Stenting for the Cardiologist,* Martin Dunitz, Ltd Publishing, 1999

Heuser RR, Henry M: *Peripheral Vascular Interventions,* Martin Dunitz, Ltd Publishing; March 2002

TEXTBOOK CHAPTERS:

Heuser RR: Coronary angioplasty for acute mitral regurgitation due to myocardial infarction. In: *Ischemic Mitral Incompetence.* Vetter HO, Hetzer R, Schumtlzer H, eds. New York, Springer Verlag, 1991:99-114.

Murphy-Chutorian D, Knopf W, Moses J, **Heuser RR**: Selected clinical cases using the eclipse laser angioplasty system. In: *Primer of Laser Angioplasty*, 2nd ed., Ginsburg R, Geschwind H, eds. Futura Publishing Co., 1991:309-324.

Heuser RR: Experience with different coronary stents. In: *Endoluminal Stenting.* Sigwart U, ed. London, W.B. Saunders Company Ltd., 1996:338-345.

Heuser RR: Peripheral stenting for the cardiologist. In: *Frontiers in Interventional Cardiology.* Beyar, Keren, Leon M, Serruys P, eds. London, Martin Dunitz Limited, 1997:377-382.

Erbel R, O'Neil W, **Heuser RR**: Long Lesion. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:48-53.

Heuser RR, Schatz R, Kimura T: Tortuous RCA. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:76-80.

Heuser RR, Schatz R, Kimura T: Tortuous Circumflex. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:81-87.

Heuser RR, Kern M: Residual stenosis: Vein Graft. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:549-551.

Nobuyoshi M, **Heuser RR**, Morice MC: New filling defects. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:555-557.

Heuser RR, Schatz R, Nobuyoshi M: Stent: Filling Defects. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:599-600.

Heuser RR, Holmes D, Roubin G: Free Perforation. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:615-617.

Heuser RR, Holmes D, Roubin G: Contained Perforation. In: *Tough Calls in Interventional Cardiology.* Safian RD, Freed M, eds. Birmingham, MI, Physician's Press, 1997:618-620.

Heuser RR, Lass, T, Prebil B, Reid DB: Computerized three-dimensional intravascular reconstruction. In: *Coronary Stenosis Morphology: Analysis and Implication.* Klein LW, ed. Chicago, IL, Kluwer Academic Publishers, 1997;103-120.

Heuser RR, Lopez AN: Introduction. In: *Peripheral Vascular Stenting for Cardiologists* Martin Dunitz Ltd. 1999:1-4.

Woodfield SL, **Heuser RR**: Angiographic anatomy of the peripheral vasculature and the noninvasive assessment of peripheral vascular disease. In: *Peripheral Vascular Stenting for Cardiologists* Martin Dunitz Ltd. 1999:5-16.

Heuser, RR, Gupta N, Lopez AN: AVE Stents. In: *Strategic Approaches in Coronary Interventions, Second Edition,* Lippincott Williams & Wilkins Publishers, 2000.

Heuser RR, Cordero-Yordan H: Carotid Artery Interventions. In: *Practical Handbook of Advanced Interventional Cardiology,* Nguyen T, Saito S, Hu D, Feldman T, Armonk, New York, Futura Publishing Company; In press.

Heuser RR: *PTFE-Covered Stents*. In: Handbook of Local Drug Delivery, Martin Dunitz Ltd. Publishing; in press.

Heuser RR, Underwood PL: *Covered Stents in Peripheral Vascular Diseases*. In: Textbook of Vascular Stenting Interventions: in press.

Heuser RR: *Certification and Training in Peripheral Vascular Intervention.* In: Textbook of Vascular Stenting Interventions: in press.

Cordero H, **Heuser RR**: *The cardiologist and peripheral intervention*. In: Practical Interventional Cardiology 2nd Edition, Martin Dunitz Ltd, Publishing: 2002:349-359.

White CW, **Heuser RR**: *The Covered Stent-Graft: Treatment of an Arteriovenous Fistula*. In: Fifty Cases in Peripheral Intervention. Martin Dunitz Ltd. Publishing: 2002:71-73.

ABSTRACTS:

Fuchs RM, **Heuser RR**, Brinker JA: Limitations of pulmonary capillary wedge V waves in diagnosing mitral regurgitation. Presented at XI InterAmerican Congress of Cardiology; September 1980.

Heuser RR, Brinker JA: Acute effects of protamine of cardiac function. Circulation 1980; 62(3): I-II.

Heuser RR, Brinker JA: Cardiac catheterization in aortic stenosis: "A Necessary Evil". Clinical Research 1981; 29:206A.

Alexander E, **Heuser RR**, Weiss JL, Firestein GS, Leitl G, Wagner Jr HN, Stevens MB, Becker LC: Sclerodermal heart disease: Evidence for cold induced abnormalities of myocardial perfusion and function. Circulation 1981; 64(4): IV-24.

Heuser RR, Becker LC, Flaherty J: Extensive myocardial infarction associated with minor electrocardiographic abnormalities: Value of admission scintigraphy. Circulation 1981; 64(4):IV-85.

Heuser RR, Goss JE, Ramo BW, Raff GL, Maddoux GL: Coronary angioplasty in Albuquerque: Report of the first large series and preliminary follow-up. Presented at the American College of Physicians, Albuquerque, New Mexico; December 1984.

Heuser RR, Goss JE, Ramo BW, Raff GL, Maddoux GL: Coronary angioplasty in patients with acute mitral regurgitation due to myocardial infarction: A nonsurgical treatment to preserve mitral valve integrity. Presented at the American Heart Association Meeting, Washington, DC; November 1985.

Heuser RR, Maddoux GL, Goss JE, Ramo BW, Raff GL: Treatment of cardiogenic shock with percutaneous coronary angioplasty: The therapy of choice. Presented at the American College of Cardiology Meeting, Atlanta, Georgia; March 1986.

Heuser RR, Maddoux GL, Goss JE, Ramo BW, Raff GL, Shadoff N: Coronary angioplasty in the elderly: A low risk option. Presented at the World Congress of Cardiology, Washington, DC; September 1986.

Heuser RR, Goss JE, Ramo BW, Raff GL, Maddoux GL, Shadoff N: Repeat coronary angioplasty: A highly successful and low risk procedure. Presented at the World Congress of Cardiology, Washington, DC; September 1986.

Raff GL, **Heuser RR**, Maddoux GL, Goss JE, Ramo BW, Archuleta B: Thallium treadmill testing accurately predicts restenosis following percutaneous transluminal coronary angioplasty. Presented at the World Congress of Cardiology, Washington, DC; September 1986.

Leatherman GF, Goss JE, Ramo BW, Raff GL, Maddoux GI, **Heuser RR**, Shadoff N, Blake K: Bucindolol improves exercise tolerance and cardiac function in patients with congestive heart failure. Presented at American College of Physicians Meeting, Albuquerque, New Mexico; December 1989.

Heuser RR, Goss JE, Ramo BW, Raff GL, Maddoux GI, Shadoff N, Leatherman GF, Blake K: A Randomized, double-blind trial of recombinant human superoxide dimutase (h-SOD) in patients undergoing PTCA for acute MI. Presented at the American College of Physicians Meeting, Albuquerque, New Mexico; December 1989.

Heuser RR, Goss JE, Ramo BW, Raff GL, Maddoux GI, Shadoff N, Leatherman GF, Blake K: Laser-assisted coronary angioplasty: Report of initial experience. Presented at the American College of Physicians Meeting, Albuquerque, New Mexico; December 1989.

Blake K, Goss JE, Ramo BW, Raff GL, Maddoux GL, **Heuser RR**, Shadoff N, Leatherman GF: Adenosine for acute treatment of SVT. Presented at the American College of Physicians Meeting, Albuquerque, New Mexico; December 1989.

Werns S, Brinker JA, Gruber J, Rothbaum D, **Heuser RR**, George B, Burwell L, Kereiakes D, Mancini GB, Flaherty J: A Randomized double-blind trial of recombinant human superoxide dismutase (h-SOD) in patients undergoing PTCA for acute MI. Circulation 1990 (IV):11-113.

Heuser RR, Schatz RA, Diethrich EB, Ponder R, Waters DB, Skeete R: Placement of the Palmaz balloon-expandable intraluminal stent in iliac arteries: A single center experience. Radiology 1991;181 (supple):295.

Heuser RR, Diethrich EB, Waters DB: Abdominal aortic stenosis: Application of Endovascular stents. Radiology 1991;181(supple):295.

Leon MB, Ellis SG, Pichard AD, Baim DS, **Heuser RR**, Schatz RA: Stents may be the preferred treatment for focal aortocoronary vein graft disease. Circulation 1991;84 (supple II): II-249.

Heuser RR, Dorsey R, Mehta S: The "Smart Needle" - a new device for vascular access. Presented at Congres Internationale d'Angiologie, Paris, France; April 1991.

Heuser RR, Mehta S, Ponder R: Stent implantation for stenosis in saphenous vein bypass grafts. Presented at Congres Internationale d'Angiologie, Paris, France; April 1991.

Ravi R, **Heuser RR**, Diethrich EB, Mehta S, Ponder R: Application of endovascular stents in the abdominal aorta. Presented at Congres Internationale d'Angiologie, Paris, France; April 1991.

Mehta S, **Heuser RR**, Siegel RM, Willoughby S: Initial report of a new, pulsed, solid-state laser system for percutaneous coronary angioplasty. Presented at Congres Internationale d'Angiologie, Paris, France; April 1991.

Mehta S, **Heuser RR**, Ponder R: Use of the Palmaz-Schatz balloon-expandable intracoronary stent for the treatment of coronary artery disease. Presented at the American College

of Chest Physicians, Arizona Chapter, Tucson, Arizona; September 1991.

Morton JK, Segal J, Ofili E, **Heuser RR**, Scott N, Aguirre F, St. Vrain J, Labovitz A, FLOMAP Study Group, SLU: A new method for quantitating coronary collateral flow in patients during coronary angioplasty using the Doppler guidewire. (poster) Presented at the American Heart Association Meeting, Anaheim, California; November 1991.

Heuser RR: Use of Holmium: YAG laser in coronary disease. Presented at the International Society for Optical Engineering – Biomedical Optics 1991. Los Angeles, California; January 1992.

Heuser RR, Strumpf RK, Walker CM, Cleman MW, Schatz RA: Coronary stenting in unstable angina: No greater risk than in stable angina. The Journal of the American College of Cardiology 1992;19:178A.

Whitlow PL, Gaspard P, Kent KM, Baim DS, Chapman JB, **Heuser RR**, Knopf WK: Improvement of coronary dissection with a removable flow support catheter: Acute results. The Journal of the American College of Cardiology 1992; 19:217A.

Teirstein PS, Schatz RA, Rocha-Singh KJ, Wong SC, Strumpf RK, **Heuser RR**: Coronary stenting with angioscopic guidance. The Journal of the American College of Cardiology 1992; 19:223A.

Donohue TJ, Kern MJ, Aguirre FV, Bell C, Penick D, Segal J, Ofili E, **Heuser RR**: Determination of the hemodynamic significance of angiographically intermediate coronary stenosis by intracoronary Doppler flow velocity. The Journal of the American College of Cardiology 1992; 19:242A.

Leon MB, Kent KM, Baim DS, Walker CM, Cleman MW, Buchbinder M, **Heuser RR**, Curry C, Schatz RA, JJIS Stent Investigators: Comparison of stent implantation in native coronaries and saphenous vein grafts. The Journal of the American College of Cardiology 1992; 19-263A.

Heuser RR, Diethrich EB, Strumpf , RK, Ponder R: Chronic iliac occlusions: Palmaz stents are the treatment of choice. Circulation 1992; 86(supple):I-634.

Heuser RR, Strumpf RK: Coronary stenting of ostial coronary artery stenosis: Intravascular ultrasound guidance. Presented at Cardiostim 1992, Nice, France; June 1992.

Heuser RR, Strumpf RK: The use of angioscopy with coronary stenting. Presented at Cardiostim 1992, Nice, France; June 1992.

Heuser RR, Diethrich EB, Strumpf RK, Ponder R: Chronic iliac occlusions: Intraluminal stents are the treatment of choice. Presented at XIV Congress of European Society of Cardiology, Barcelona, Spain; August 1992.

Heuser RR, Strumpf RK: Angioscopy with coronary stenting: Is it helpful? Presented at XIV Congress of European Society of Cardiology, Barcelona, Spain; August 1992.

Heuser RR: Intravascular coronary artery stents. Presented at the American College of Surgeons, postgraduate courses, New Orleans, Louisiana; October 1992.

Heuser RR, Brinker JA, Weiner BH for Strecker Stent Investigators: Strecker coronary stent: Initial multicenter experience. The Journal of the American College of Cardiology 1993; 21:293A.

Fischman D, Savage M, Leon M, Schatz RA, **Heuser RR**, Goldberg S: Acute and long-term results of coronary stenting for complex intimal dissections following balloon angioplasty. The Journal of the American College of Cardiology 1993; 21:178A.

Schatz RA, Penn IM, Baim DS, Nobuyoshi M, Colombo A, Ricci DR, Cleman MW, Goldberg S, **Heuser RR**, Almond D, Fish D, Moses J, Gallup D, Detre K, Leon MB for the STRESS Investigators: Stent Restenosis Study (STRESS) analysis of in-hospital results. Circulation 1993; 88:I-594.

Heuser RR, Hardigan K, Strumpf R, Eagan J, Aultman R, Prebil B, Waters K: Single Center Palmaz "Biliary" Stent Experience in Coronary Arteries and Saphenous Vein Grafts. Circulation 1993; 88:(4) Part II.

White CJ, Ramee SR, Collins TJ, Jain SP, Escobar A, Soni D, Bass TA, **Heuser RR**, Teirstein PS, Bonan R, Nesto RW, Walter PD, Smalling RW, Knopf WD: Angioscopically detected coronary thrombus correlates with adverse PTCA outcome. Circulation 1993; 88:I-596.

Kussmaul WG, Buchbinder M, Whitlow PL, Aker UT, **Heuser RR**, King SB, Sandza JG, Kensey KR: Randomized trial of a new hemostatic puncture closure device. Circulation 1993; 88:I-72.

Heuser RR, Hardigan KR, Strumpf RK, Eagan JT: Single-center Palmaz biliary stent experience in coronary arteries and saphenous veins. Circulation 1993; 88:I-308.

Fortuna R, **Heuser RR**, Garratt KN, Schwartz R, Buchbinder M: Wiktor intracoronary stent: Experience in the first 101 vein graft patients. Circulation 1993; 88:I-505.

Teirstein PS, Schatz RA, Rocha-Singh KJ, DeNardo SJ, Morris N, Strumpf RK, **Heuser RR**: Angioscopy of coronary stents at follow-up. The Journal of the American College of Cardiology 1993; 21:134A.

Thompson MA, Brinker JA, **Heuser RR**, Weiner BH, Hess K, Ross AM, Segal J, The George Washington University Quantitative Analysis Core Laboratory for the Strecker Stent Investigators: Balloon-expandable stent size versus inflation pressure: The Strecker experience. The Journal of the American College of Cardiology 1993; 21:293A.

Heuser RR, Hardigan K, Strumpf R, Eagan J, Aultman R, Prebil B, Waters K: Single Center Palmaz "Biliary" Stent Experience in Coronary Arteries and Saphenous Vein Grafts. Presented at the American Heart Association Scientific Session; October 1993.

Heuser RR, Strumpf RK, Ramirez-Cardenas J, Schmidt J: Experience with seven stent models in the coronary arteries and vein grafts. Journal Interventional Cardiology 1994; 7:90.

Fischman D, Savage M, Leon MB, Schatz R, Baim D, Penn I, Detre K, **Heuser RR**, Ricci D, Fish D, Rake R, Gebhardt S, Goldberg S for the STRESS Investigators, Jefferson Medical College, Philadelphia, PA: Acute and late angiographic results of the Stent Restenosis Study (STRESS). The Journal of the American College of Cardiology 1994 (special issue): 60A.

Segal J, Reiner JS, Thompson MA, Brinker JA, **Heuser RR**, Weiner BH, Ross AM, The George Washington University Quantitative Analysis Core Laboratory for the Strecker Stent Investigators: Residual stenosis following coronary stenting do not predict restenosis in the Strecker stent. The Journal of the American College of Cardiology 1994 (special issue):134A.

Carrozza JP, Kuntz RE, Leon MB, Schatz RA, Brinker J, Chuang YC, **Heuser RR**, Baim DS: Demographic, angiographic and procedural factors associated with late angiographic outcome in the STRESS Trial: A multivariable analysis. Circulation 1994; 90:I-18.

Garratt KN, White CJ, Buchbinder M, Whitlow PK, **Heuser RR** on behalf of the American Wiktor Stent Investigators: Wiktor stent placement for unsuccessful coronary angioplasty. Circulation 1994; 90:I-279.

Heuser RR, Cleman M, Cabin H, Wong SC, Chuang YC, Bailey S, Nobuyoshi M, Almond D, Schatz R: The LAD subgroup in the Stent Restenosis Study: Early and late angiographic and clinical outcomes. Circulation 1994; 90:I-323.

Savage M, Fischman D, Rake R, Hirshfeld J, Penn I, **Heuser RR**, Shaknovich A, Moses J, Ricci D, Goldberg S: Effect of lesion morphology on angiographic outcome after balloon angioplasty and coronary stenting: Results from the STRESS Trial. Circulation 1994; 90:I-324.

Kussmaul WG, Sandza JG, **Heuser RR** for the Angio-Seal™ in patients at high risk of bleeding complications. Catheterization and Cardiovascular Interventions 1994; 32:98.

Sketch Jr. MH, Wong SC, Chuang YC, Phillips HR, **Heuser RR**, Savage M, Stack RS, Baim DS, Schatz RA, Leon MB for the JJIS Stent Investigators: Progressive deterioration in late (2-Year) clinical outcomes after stent implantation in saphenous vein grafts: The multicenter JJIS experience. The Journal of the American College of Cardiology 1995 (special issue): 79A.

Savage M, Douglas J, Fischman D, Fenton S, King S, Pepine C, Bailey S, Overlie P, Werner J, Leon M, **Heuser RR**, Brinker J, Buchbinder M, Smalling R, Snead D, Rake R, Gebhardt S, Kerensky R, Wargovich T, Goldberg S, SAVED Trial Investigators: Coronary stents versus balloon angioplasty for aortocoronary saphenous vein bypass graft disease: Interim results of a randomized trial. The Journal of the American College of Cardiology 1995 (special issue):79A.

Wong SC, Chuang YC, Detre K, Pichard AD, Schatz RA, **Heuser RR**, Kent KM, Leon MB: Is the anti-restenosis effect of stent (vs PTCA) greater in LAD vessels? A subgroup analysis of the Stent Restenosis Study. The Journal of the American College of Cardiology 1995 (special issue):374A.

Primack DS, **Heuser RR**, Kuntz RE, Waters K, Swiderski K: Coronary stenting performed via brachial access is more economical. Presented at the American College of Cardiology 44th Annual Scientific Session, New Orleans, Louisiana; March 1995.

Primack DS, **Heuser RR**, Kuntz RE, Waters K, Swiderski K: Coronary stenting performed via brachial access is more economical. Presented at the 18th Annual Meeting of the Society for Cardiac Angiography and Interventions, Orlando, Florida; May 1995.

Heuser RR, Reynolds GT, Papazoglou C, Diethrich EB: Endoluminal grafting for percutaneous aneurysm in an aortocoronary saphenous vein graft: The first human experience. Presented at the 18th Annual Meeting of the Society for Cardiac Angiography and Interventions, Orlando, Florida; May 1995.

Garratt KN, Schwartz RS, Holmes Jr DR, White CJ, Buchbinder M, Whitlow PL, **Heuser RR** on behalf of the American Wiktor Stent Investigators: Placement of Wiktor coronary stents for management of unsuccessful coronary angioplasty: The American Experience. Presented at the 1st International Meeting on Interventional Cardiology, Jerusalem, Israel; June 1995. The Journal of Invasive Cardiology 1995; 7 (supple)35C.

Heuser RR, Reynolds GT, Papazoglou C, Diethrich EB, Mukherjee R: Compassionate endoluminal grafting for percutaneous aneurysm exclusion in aortocoronary saphenous vein

grafts. Presented at the XVIIth Congress of the European Society of Cardiology, Amsterdam, The Netherlands; August 1995. Journal of Endovascular Surgery 1995; 2:81-88.

Heuser RR, Wong SC, Chuang YC, Detre K, Pichard AD, Schatz RA, Kent KM, Leon MB for the STRESS investigators: The LAD subgroup in the Stent REStenosis Study (STRESS): The most pronounced anti-restenosis effect of stenting. Presented at the XVIIth Congress of the European Society of Cardiology, Amsterdam, The Netherlands; August 1995.

Heuser RR, Reynolds GT, Papazoglou C, Diethrich EB, Mukherjee R: Compassionate endoluminal grafting for percutaneous treatment of aortocoronary SVG disease. The Journal of the American College of Cardiology 1996; 27:179A.

Savage M, Fischman D, Rake R, Schatz R, Penn I, Nobuyoshi M, Moses J, **Heuser RR**, Gebhardt S, Goldberg S for the STRESS Trial Investigators: Elective coronary stenting verses balloon angioplasty in smaller native coronary arteries: Results from STRESS. The Journal of the American College of Cardiology 1996; 27:253A.

Leon MB, Ellis SG, Moses J, King SB, **Heuser R**, Kent KM, Goldbert S, Fischman D, Senerchia C, Lanoue AS, Kuntz RE: Interim Report from the Reduced Anticoagulation Vein Graft Stent (RAVES) Study. Presented at the American Heart Association 69th Scientific Session, New Orleans, Louisiana; November 1996.

Savage M, Fischman D, Slota P, Rake R, Leon M, Schatz R, Moses J, Penn I, Nobuyoshi M, **Heuser RR**, Goldberg S: Coronary intervention in the diabetic patient: Improved outcome following stent implantation versus balloon angioplasty. Presented at the American College of Cardiology 46th Annual Scientific Session, Anaheim, California; March 1997.

Dean LS, **Heuser RR**, Moore PB, Rogers EW, Roubin GS, Leon MB, Voorhees WD, Holmes Jr DR, O'Shoughnessy CD, Zidar JP: Stenting in small vessels: A re-evaluation using the GR-II intracoronary stent, a Cook Registry Study. Presented at the American College of Cardiology 46th Annual Scientific Session, Anaheim, California; March 1997.

Heuser RR: Live Demonstrations. Presented at the 1997 Japanese Society of Interventional Cardiology Live Demonstration Symposium, Kokura, Japan; May 1997.

Heuser RR: Influence of minimally invasive coronary artery bypass surgery. Presented at the XIXth Congress of the European Society of Cardiology, Stockholm, Sweden; August 1997.

Heuser RR, Kuntz RE, Lansky AJ, Whitlow PL, Sanfian RD, Yeung AC, Senerchia C, Cutlip DE, Pino-Mauch B, Pedan A: The SMART Trial: Acute outcome indicates superior efficacy with the AVE Stent. Presented at the XIXth Congress of the European Society of Cardiology, Stockholm, Sweden; August 1997.

Heuser RR, Kuntz R, Popma J, Pino-Mauch B, Miller R, Yeung A, Badger R: The SMART Trial: 30-day outcome indicates superior efficacy with the AVE Stent. Presented at the Transcatheter Cardiovascular Therapeutics Symposium, Washington, DC; September 1997.

Heuser RR: Influence of modern bypass surgery on PTCA. Presented at 20 Years of PTCA - Back to the Cradle, Zurich, Switzerland; September 1997.

Heuser RR: An overview of new stent designs: Lesion specific stenting. Presented at Coronary Interventions 1997, LaJolla, California; October 1997.

Heuser RR: Covered stents: Clinical needs, future prospects. Presented at Coronary Interventions 1997, LaJolla, California; October 1997.

Heuser RR, Kuntz RE, Lansky AJ, Whitlow PL, Safian RD, Yeung AC, Senerchia C, Cutlip DE, Pino-Mauch B, Pedan A: The SMART Trial: Acute outcome indicates superior efficacy with the AVE Stent. American Heart Association 70th Scientific Sessions, Orlando, Florida; November 1997.

Heuser RR: Is carotid artery PTA superior to surgery? Presented at the International Course on Interventional Cardiology, Frankfurt, Germany; December 1997.

Heuser RR, Kuntz R, Popma J, Pino-Mauch B, Miller R, Yeung A, Badger R: The SMART Trial: 30-day outcome indicates superior efficacy with the AVE Stent. Presented at the American College of Cardiology 47th Annual Scientific Session, Atlanta, Georgia; April 1998.

Heuser RR, Kuntz R, Lansky, A, Kalon KLH, Reduto L, Badger R, Iannone LA, Whitlow P, Vlietstra R: A comparison of the Long AVE Micro™ Stent II and the Palmaz-Schatz® Stent: A SMART trial registry. Presented at the American College of Cardiology 47th Annual Scientific Session, Atlanta, Georgia; April 1998.

Heuser RR, Houser F, Battaglia S, Tarkington L, Simon A, Culler S, Becker E: Repeat procedure rates in percutaneous interventions: Is there added benefit of atherectomy or stenting? Presented at Transcather Cardiovascular Therapeutics, Washington, DC; October 1998.

Heuser RR, Lopez AN, Stoerger H, Reifart N: Coronary artery application of an endoluminal polytetrafluorethylene stent graft: Two center experience with the JOMED® JoStent®. Presented at American Heart Association, Dallas, Texas; November 1998.

Ramee SR, Baim DS, Popma JJ, Ho KKL, Cutlip DE, Lanoue AS, Dandreo KJ, Schatz RA, Sharma SK, Kuntz RE, **Heuser RR**: A randomized, prospective, multi-center study comparing intracoronary Urokinase to Rheolytic thrombectomy with the POSSIS AngioJet Catheter for intracoronary thrombus: Final results of the VeGAS 2 Trial. Presented at American Heart Association, Dallas, Texas; November 1998.

Heuser RR, Lopez AN: Coronary Artery Disease Revascularization with the JOMED JoStent®: A Two Center Experience. Presented at American College of Cardiology, New Orleans, Louisiana; March 1999.

Lansky AJ, Popma JJ, Mehran R, Hanzel G, Cutlip D, Ho KK, Proctor B, Happi JA, Kuntz RE, Baim DS, **Heuser RR**, Midei M, O'Shaughnessy C, Leon MB: Tubular Slotted Stents: A "Breakthrough Therapy" for Women Undergoing Coronary Interventions. Pooled Results from the STARS, ACSENT, SMART, and NIRVANA Randomized Clinical Trials. Presented at American College of Cardiology, New Orleans, Louisiana; March 1999.

Oesterle SN, Yeung A, Ali N, Dean LS, **Heuser RR**, Knopf WD, Masden R, Ramee SR, Reeder GS, Resar J, Sanborn TA, Schaer GL, Schofield PM: The CardioGenesis Percutaneous Myocardial Revascularization (PMR) Randomized Trial: Initial Clinical Results. Presented at American College of Cardiology, New Orleans, Louisiana; March 1999.

Heuser RR: New Findings of PMR and Gene Therapy. Presented at 4th Asian-Pacific Society of Interventional Cardiology Conference and 8th Live Demonstration in Kokura, Kokura, Japan; May 1999.

Heuser RR: The Use of Covered Coronary Stents: A new Therapy in Evolution. Presented at 4th Asian-Pacific Society of Interventional Cardiology Conference and 8th Live Demonstration in Kokura, Kokura, Japan; May 1999.

Heuser RR: Radiofrequency Enhancement of Intramyocardial Gene Therapy. Presented at the Second Annual Symposium Angiogenesis and DMR Agenda, Washington, DC; June 1999.

Heuser RR: Covered Stents for Coronary Artery Disease: Early Results of Clinical Trials. Presented at the Sixth Annual Mayo Interventional Cardiology Symposium, Napa Valley, California; July 1999.

Heuser RR: Peripheral Vascular Disease Management: New Devices, New Drugs, New Approaches. Presented at the Sixth Annual Mayo Intervention Cardiology Symposium, Napa Valley, California; July 1999.

Heuser RR: Radiofrequency PMR: A Unique System for Simultaneous Radiofrequency PMR and Gene Therapy. Presented at the XXIst Congress of the European Society of Cardiology, Barcelona, Spain; August 1999;20;2828.

Heuser RR: Do Coronary Stents Improve Clinical Outcomes? A retrospective study comparing stent device utilization and adverse outcomes. Presented at the XXIst Congress of the European Society of Cardiology, Barcelona, Spain; August 1999.

Oesterle SN, Sanborn TA, Ali N, Resar J, Ramee SR, **Heuser RR**, Dean L, Knopf W, Schofield P, Schaer GL, Reeder G, Masden R, Yeung AC, Burkhoff D: Percutaneous transmyocardial laser revascularization for severe angina: the PACIFIC randomized trial. Presented at the 72nd Scientific Session American Heart Association, Atlanta, Georgia, November 1999.

Sameer Mehta, **Heuser RR**, Salvatore BL, Simon AW, Culler SD, Becker ER: Evolving Patterns of Coronary Senting: Report from a Large National Database. Presented at the 49th Annual Scientific Session American College of Cardiology, March 2000.

Heuser RR: Future of Covered Stents and Endoluminal Grafts. Presented at the GET International Endovascular Peripheral Course in Monaco; May 2000.

Heuser RR, Heilbrunn S, Fogarty TJ, Motarjeme A: Establishing an Integrated Vascular Center. Presented at the Eighth New Devices Seminar for the Cardiac and Peripheral Vascular Laboratories in Orlando, Florida; July 2000.

Heuser RR, Covered Stents: New Options & Strategies. Presented at the Eighth New Devices Seminar for the Cardiac and Peripheral Vascular Laboratories in Orlando, Florida; July 2000.

Heuser RR, Waksman R, White CJ: Advanced Coronary Workshop: The experts discuss techniques and equipment on the Progress Occurring with Stent Grafts & Brachytherapy for the Coronary and Bypass Graft Circulation. Presented at the Eight New Devices Seminar for the Cardiac and Peripheral Vascular Laboratories in Orlando, Florida; July 2000.

Heuser RR, Cordero H, Underwood PL, Schroeder WS, Weirick BA, Hatler CW: Single Center Experience with OCR Guidance in the Treatment of Chronic Total Occlusions (CTO). Submitted to Transcatheter Cardiovascular Therapeutics; September 2001.

Cordero H, Underwood PL, Schroeder WS, Weirick BA, Hatler CW, **Heuser RR**: Fiber Optic Guidance Technology in the Treatment of Chronic Total Occlusions: Initial Experience. Presented at 12th Annual Symposium Transcatheter Cardiovascular Therapeutics; October 2000.

Laskey WK, **Heuser RR**, Suntharalingam M, Bass TA, Silber S, Rutherford BD, Wilmer C, Berke AD, Snell RJ, Popma J, Kuntz RE: Effects of ^{90}SR/^{90}Beta Radiation on Diabetic Patients with In-Stent Restenosis. Presented at AHA November 2000.

Heuser RR, Cordero H, Underwood PL, Schroeder WS, Weirick BA, Hatler CW: OCR Can Be Used to Safely Treat Chronic Total Occlusions. Presented at AHA; November 2000.

Heuser RR, Cordero H, Underwood PL, Schroeder WS, Weirick BA, Hatler CW: Single Center Experience with OCR Guidance in the Treatment of Chronic Total Occlusions (CTO). Circulation October 23, 2001; Vol 104 (17) 1978.

Heuser RR, Cordero H, Schroeder W, Weirick BA, Hatler CW, Underwood PL: Fiberoptic Guidance System for Treatment of Chronic Total Occlusions: Single Center Experience. Presented at ACC 2001; March 2001.

Heuser RR, Lasky W, Bonan R, Lansky A: B-Radiation in Lesions Longer Than 20 Millimeters: A START 40/20 Subgroup Analysis. TCT 2001: September 2001.

Heuser RR, Underwood PL, Schroeder W, Weirick BA, Hatler CW: Experience with OCR Guidance in the Treatment of Chronic Total Occlusions. TCT 2001: September 2001.

PA Morales, **RR Heuser,** W Laskey, R Bonan, AJ Lansky, JJ Popma: Treating In-Stent Restenosis in Long Coronary Lesions. Presented at the 51st Annual Scientific Session American College of Cardiology; March 2002.

PA Morales, **RR Heuser**, EA Weirick, CW Hatler: Predicting Success in Crossing Chronic Total Occlusions With a New Guidewire. Presented at the 51st Annual Scientific Session American College of Cardiology; March 2002.

WK Laskey, M Suntharalingam, J Popma, **R Heuser**, B Rutherford, P Teirstein, A Lansky, R Kuntz, R Bonan: Efficacy of SR-90 Beta Radiation for the Treatment of In-Stent Restenosis: 24-Month Clinical Outcomes from the Stents And Radiation Therapy Trial (START). Presented at the 51st Annual Scientific Session American College of Cardiology; March 2002.

P.A. Morales, A. Reese, W. Schroeder, **R.R. Heuser**, New Treatment for Chronic Total Occlusions of Femoral Arteries. Presented at the Fourteenth Annual Symposium Transcatheter Cardiovascular Therapeutics; September, 2002

AWARDS & HONORS:

Columbia/HCA Cardiovascular Management Network - 1998 Cardiologist of the Year

PATENTS:

1. Method and Apparatus for Treating Body Tissues and Bodily Fluids; Patent granted December 12, 2000 Number: 6,159,197
2. Hot Tip Catheter; Patent granted February 20, 2001 Number: 6,190,379
3. Embolism Prevention Device; Patent granted April 2, 2002 Number: 6,364,900
4. Catheter apparatus and Method for Arterializing a Vein; Patent granted October 15, 2002 Number 6,464,665
5. Methods and apparatus for treating body tissues and bodily fluid vessels; Patent granted October 15, 2002 Number: 6,464,681
6. Catheter for Thermal Evaluation of Arteriosclerotic Plaque; Patent granted March 25, 2003 Number: 6,536,949
7. Small Diameter Snare; Patent granted April 29, 2003 Number: 6,554,842

EXHIBIT B

DISCLOSURES
APPLICATION SERIAL NO. 09/064,000

PAGE 20, LINE 10 – PAGE 21, LINE 15

Growth factors can be utilized to induce the growth of "hard tissue" or bone and "soft tissues" like ectodermal and mesodermal tissues. As used herein, the term growth factor encompasses compositions and living organisms which promote the growth of hard tissue, such as bone, or soft tissue, in the body of a patient. The compositions include organic and inorganic matter. The compositions can be genetically produced or manipulated. The living organisms can be bacteria, viruses, or any other living organism which promote tissue growth. By way of example and not limitation, growth factors can include platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (acidic/basis (FGF a,b), interleukins (IL's), tumor necrosis factor (TNF), transforming growth factor (TGF-B), colony-stimulating factor (CSF), osteopontin (Eta-1 OPN), platelet-derived growth factor (PDGF), interferon (INF), bone morphogenic protein 1 (BMP-1), and insulin growth factor (IGF). Recombinant and non-recombinant growth factors can be utilized as desired. Bacteria or viruses can, when appropriate, be utilized as growth factors. For example, there is a bacterial hydrophilic polypeptide that self-assembles into a nanometer internal diameter pore to build a selective lipid body. Various enzymes can be utilized for the synthesis of peptides which contain amino acids that control three-dimensional protein structure and growth. Growth factors can be applied in gels or other carriers which regulate the rate of release of the growth factors and help maintain the growth factors and the carrier, at a desired location in the body. Time release capsules, granules, or other carriers containing growth factor can be activated by tissue pH, by enzymes, by ultrasound,

by electricity, by heat, by selected *in vivo* chemicals or by any other selected means to release the growth factor. The carrier can be resorbable or non-resorbable. Or, the growth factor itself can be activated by similar means. Either the carrier or the growth factor can mimic extracellular fluid to control cell growth, migration, and function. The growth factor can be administered orally, systemically, in a carrier, by hypodermic needle, through the respiratory tract, or by any other desired method. The growth factor an also be administered into a capsule or other man-made composition or structure placed in the body. While administration of the growth factor is presently usually localized in the patient's body, circumstances may arise where it is advantageous to distribute a growth factor throughout the patient's body in uniform or non-uniform concentrations. An advantage to growth factors is that they can often, especially when in capsule form or in some other containment system, be inserted to a desired site in the body by simply making a small incision and inserting the growth factor. The making of such small incision comprises minor surgery which an often be accomplished on an out-patient basis. The growth factors can be multifactorial and nonspecific.

PAGE 37, LINES 19-25

Multifactorial and nonspecific cells (such as stem cells and germinal cells) can provide the necessary in vivo and in vitro cascade of genetic material once an implanted master control gene's transcription has been activated. Likewise, any host cell, clone cell, cultured cell, or cell would work. Genetic switches (such as the insect hormone ecdysone) can be used to control genes inserted into humans and animals. These gene switches can also be used in cultured cells or other cells. Gene switches govern whether a gene is on or off making possible precise time of gene activity.

PAGE 44, LINE 19 – PAGE 46, LINE 16

Genetic material comprising a portion of a gene, a gene, genes, a gene product (i.e., a composition a gene causes to be produced like, for example, an organ-producing growth factor), growth factor, or an ECM (extracellular matrix) can be used in or on the body to grow an organ to tissue. For example, the vascular epithelial growth factor gene (VEGF) or its growth factor equivalent can be inserted into the body to cause an artery to grow. When insertion of a gene, portion of a gene, gene product, growth factor, or ECM *in vivo* or *ex vivo* is referred to herein in connection with any of the implant techniques of the invention, it is understood that a cell nutrient culture(s), physiological nutrient culture(s), carrier (s), enhancer(s), promoter(s), or any other desired auxiliary component(s) can be inserted with the gene or at the same location as the gene, growth factor, ECM, etc.

An artery is an organ from the circulatory system. An artery can be grown in the heart, legs, or other areas by injecting a gene or other genetic material into muscle at a desired site. Size, vascularity, simplicity of access, ease of exploitation, and any other desired factors can be utilized in selecting a desired site. The gene is one of several known VEGF genes which cause the production of vascular endothelial growth factors. Several VEGF genes which produce vascular endothelial growth factors are believed to exist because nature intends for there to be several pathways (i.e., genes) which enable the production of necessary growth factors. The existence of several pathways is believed important because if one of the genes is damaged or inoperative, other similar genes can still orchestrate the production of necessary growth factors. VEGF genes are used by the body to promote blood vessel growth. VEGF genes are assimilated (taken in) by muscle cells. The genes cause the muscle cells to make a VEGF protein which

promotes the growth of new arteries. VEGF proteins can be made in a lab and injected into a patient intravenously, intraluminally, or intramuscularly to promote the growth of an artery. Or, the genes (or other genetic material) can be applied with an angioplasty balloon, with the assistance of a vector, or by any other method.

It is not always desirable to grow a completely new organ. Sometimes growing a portion of an organ is desirable. For example, in some heart attacks or strokes, a portion of the heart or brain remains viable and a portion dies. An injection of a gene to form cardiac muscle and/or an injection of a gene to form an artery can be utilized to revive or replace the dead portion of the heart. The dead portion of the heart may (or may not) be used as a matrix while the new muscles and vessels grow. Thus, in this example, a partial new organ is grown in a pre-existing organ. A pacemaker may (or may not) be necessary. A second injection of a gene may (or may not) be necessary to stop cardiac muscle growth once it is completed. Portions of organs throughout the body can similarly be repaired or replaced. It may be necessary to provide gene(s) or growth factor(s) sequentially. For instance, one or more blood vessels are grown by inserting an appropriate gene or other genetic material into a selected area. Second, an appropriate gene or other genetic material is inserted in the selected area to grow a bone or other organ.

The size and shape limitation of the desired structure can come from a containment and boundary contact inhibition phenomenon or by a chemical inhibition.

A variation on the theme of growing a portion of an organ is as follows: a portion of a heart dies. The pericardium is utilized as a scaffold and seeded with cells and/or genes to grow new muscle, and genes (or other genetic material) to grow new arteries. Immediately adjacent the dead cardiac muscle, onto or into the pericardium, the appropriate cells, genes, and/or growth factors (or other genetic material) are placed. Once the new muscle and blood vessels have

grown, the function specific tissue can be applied to the damaged portion of the heart and paced, if necessary, to augment cardiac action. If the surgeon desires, the dead muscle can be removed and the new muscle and blood vessels can be surgically rotated into the excised region and secured. This probably can be done endoscopically. In essence, the pericardium is utilized to allow the new muscle wall to grow. The new muscle wall is then transplanted into the damaged heart wall. This procedure utilizes the body as a factor to grow an organ and/or tissue, after which the organ and/or tissue is transplanted to a desired region. On the other hand, the new muscle wall may integrate itself into the old wall and not require transplantation.

PAGE 47, LINE 22 – PAGE 48, LINE 15

Organs and/or tissues can be formed utilizing the patient's own cells. For example, a skin cell(s) is removed from the intraoral lining of a cheek. The cell is genetically screened to identify DNA damage or other structural and/or functional problems. Any existing prior art genetic screening technique can be utilized. Such methods can utilize lasers, DNA probes, PCR, or any other suitable device. If the cell is damaged, a healthy undamaged cell is, if possible, identified and selected. If a healthy cell can not [sic] be obtained, the damaged cell can be repaired by excision, alkylation, transition or any other desired method. A growth factor(s) is added to the cell to facilitate dedifferentiation and then redifferentiation and morphogenesis into an organ or function specific tissue. Any machine known in the art can be used to check the genetic fitness of the organ and its stage of morphogenesis. A cell nutrient culture may or may not be utilized depending on the desired functional outcome (i.e., growth of an artery, of pancreatic Islet cells, of a heart, etc.) or other circumstances. Replantation can occur at any appropriate stage of morphogenesis. The foregoing can be repeated without the patient's own

cells if universal donor cells such a [sic] germinal cells are utilized. Germinal cells do not require a dedifferentiation. They simply differentiate into desired tissues or organs when properly stimulated. Similarly, the DNA utilized in the foregoing procedure can come from the patient or from any desired source.

During reimplantation one of the patient's own cells is returned to the patient. During implantation, a cell not originally obtained from the patient is inserted on or in the patient.

In the example above, if germinal cells (and in some case, stem cells) are utilized a direct differentiation and morphogenesis into an organ can occur in vivo, ex vivo, or in vitro.

EXHIBIT C

DEFINITIONS

PAGE 20, LINE 10 – PAGE 21, LINE 15

Growth factors can be utilized to induce the growth of "hard tissue" or bone and "soft tissues" like ectodermal and mesodermal tissues. As used herein, the term growth factor encompasses compositions and living organisms which promote the growth of hard tissue, such as bone, or soft tissue, in the body of a patient. The compositions include organic and inorganic matter. The compositions can be genetically produced or manipulated. The living organisms can be bacteria, viruses, or any other living organism which promote tissue growth. By way of example and not limitation, growth factors can include platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (acidic/basis (FGF a,b), interleukins (IL's), tumor necrosis factor (TNF), transforming growth factor (TGF-B), colony-stimulating factor (CSF), osteopontin (Eta-1 OPN), platelet-derived growth factor (PDGF), interferon (INF), bone morphogenic protein 1 (BMP-1), and insulin growth factor (IGF). Recombinant and non-recombinant growth factors can be utilized as desired. Bacteria or viruses can, when appropriate, be utilized as growth factors. For example, there is a bacterial hydrophilic polypeptide that self-assembles into a nanometer internal diameter pore to build a selective lipid body. Various enzymes can be utilized for the synthesis of peptides which contain amino acids that control three-dimensional protein structure and growth. Growth factors can be applied in gels or other carriers which regulate the rate of release of the growth factors and help maintain the growth factors and the carrier, at a desired location in the body. Time release capsules, granules, or other carriers containing growth factor can be activated by tissue pH, by enzymes, by ultrasound,

by electricity, by heat, by selected *in vivo* chemicals or by any other selected means to release the growth factor. The carrier can be resorbable or non-resorbable. Or, the growth factor itself can be activated by similar means. Either the carrier or the growth factor can mimic extracellular fluid to control cell growth, migration, and function. The growth factor can be administered orally, systemically, in a carrier, by hypodermic needle, through the respiratory tract, or by any other desired method. The growth factor an also be administered into a capsule or other man-made composition or structure placed in the body. While administration of the growth factor is presently usually localized in the patient's body, circumstances may arise where it is advantageous to distribute a growth factor throughout the patient's body in uniform or non-uniform concentrations. An advantage to growth factors is that they can often, especially when in capsule form or in some other containment system, be inserted to a desired site in the body by simply making a small incision and inserting the growth factor. The making of such small incision comprises minor surgery which an often be accomplished on an out-patient basis. The growth factors can be multifactorial and nonspecific.

MEDLINE PLUS: MERRIAM-WEBSTER MEDICAL DICTIONARY
A SERVICE OF THE U.S. NATIONAL LIBRARY OF MEDICINE AND THE NATIONAL INSTITUTES OF HEALTH

> **Growth factor:** a substance (as a vitamin B_{12} or an interleukin) that promotes growth and especially cellular growth

EXHIBIT D

CLAIMS
APPLICATION SERIAL NO. 09/064,000

382. A method for producing a desired soft tissue in a body of a human patient comprising:

(a) Placing cells in said body of said human patient;

(b) Forming a bud in said body of said human patient; and

(c) Growing said desired soft tissue from said bud.

383. The method of claim 382, wherein said cells are multifactorial and non-specific.

384. The method of claim 383, wherein said cells comprise stem cells.

385. The method of claim 382 further comprising forming a new artery.

386. The method of claim 383 further comprising forming a new artery.

387. The method of claim 382, wherein said soft tissue comprises mesodermal tissue.

388. The method of claim 382, wherein said soft tissue comprises an artery.

Repair of Infarcted Myocardium by Autologous Intracoronary Mononuclear Bone Marrow Cell Transplantation in Humans

Bodo E. Strauer, MD; Michael Brehm, MD; Tobias Zeus, MD; Matthias Köstering, MD; Anna Hernandez, PhD; Rüdiger V. Sorg, PhD; Gesine Kögler, PhD; Peter Wernet, MD

Background—Experimental data suggest that bone marrow–derived cells may contribute to the healing of myocardial infarction (MI). For this reason, we analyzed 10 patients who were treated by intracoronary transplantation of autologous, mononuclear bone marrow cells (BMCs) in addition to standard therapy after MI.

Methods and Results—After standard therapy for acute MI, 10 patients were transplanted with autologous mononuclear BMCs via a balloon catheter placed into the infarct-related artery during balloon dilatation (percutaneous transluminal coronary angioplasty). Another 10 patients with acute MI were treated by standard therapy alone. After 3 months of follow-up, the infarct region (determined by left ventriculography) had decreased significantly within the cell therapy group (from 30±13 to 12±7%, $P=0.005$) and was also significantly smaller compared with the standard therapy group ($P=0.04$). Likewise, infarction wall movement velocity increased significantly only in the cell therapy group (from 2.0±1.1 to 4.0±2.6 cm/s, $P=0.028$). Further cardiac examinations (dobutamine stress echocardiography, radionuclide ventriculography, and catheterization of the right heart) were performed for the cell therapy group and showed significant improvement in stroke volume index, left ventricular end-systolic volume and contractility (ratio of systolic pressure and end-systolic volume), and myocardial perfusion of the infarct region.

Conclusions—These results demonstrate for the first time that selective intracoronary transplantation of autologous, mononuclear BMCs is safe and seems to be effective under clinical conditions. The marked therapeutic effect may be attributed to BMC-associated myocardial regeneration and neovascularization. (*Circulation*. 2002;106:1913-1918.)

Key Words: myocardial infarction □ cell transplantation, intracoronary □ angiogenesis □ bone marrow □ myogenesis

Remodeling of the left ventricle after myocardial infarction (MI) represents a major cause of infarct-related heart failure and death. This process depends on acute and chronic transformation of both the necrotic infarct region and the non-necrotic, peri-infarct tissue.[1,2] Despite application of pharmacotherapeutics and mechanical interventions, the cardiomyocytes lost during MI cannot be regenerated. The recent finding that a small population of cardiac muscle cells is able to replicate itself is encouraging but is still consistent with the concept that such regeneration is restricted to viable myocardium.[3]

In animal experiments, attempts to replace the necrotic zone by transplanting other cells (eg, fetal cardiomyocytes or skeletal myoblasts) have invariably succeeded in reconstituting heart muscle structures, ie, myocardium and coronary vessels. However, these cells fail to integrate structurally and do not display characteristic physiological functions.[4-7] Another approach to reverse myocardial remodeling is to repair myocardial tissue by using bone marrow–derived cells. Bone marrow contains multipotent adult stem cells that show a high capacity for differentiation.[8-10] Experimental studies have shown that bone marrow cells (BMCs) are capable of regenerating infarcted myocardium and inducing myogenesis and angiogenesis; this leads in turn to amelioration of cardiac function in mice and pigs.[11-14] However, procedures based on this phenomenon remain largely uninvestigated in a human clinical setting.

An investigation of one patient receiving autologous skeletal myoblasts into a postinfarction scar during coronary artery bypass grafting revealed improvement of contraction and viability 5 months afterward.[15] Autologous mononuclear BMCs transplanted in a similar surgical setting showed long-term improvement of myocardial perfusion in 3 of 5 patients and no change in 2 patients.[16] However, such studies entail a surgical approach and are therefore associated with well-known perioperative risks. Moreover, this surgical procedure cannot be used with MI. We therefore looked for a nonsurgical, safer mode for transplanting autologous cells

Received August 2, 2002; accepted August 2, 2002.

From the Department of Medicine, Division of Cardiology (B.E.S., M.B., T.Z., M.K.) and Institute for Transplantation Diagnostics and Cell Therapeutics (A.H., R.V.S., G.K., P.W.), Heinrich-Heine-University of Düsseldorf, Germany.

Correspondence to Professor Dr Bodo E. Strauer, Department of Medicine, Division of Cardiology, Heinrich-Heine-University, Moorenstr 5, 40225 Düsseldorf, Germany. E-mail Strauer@med.uni-duesseldorf.de

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/01.CIR.0000034046.87607.1C

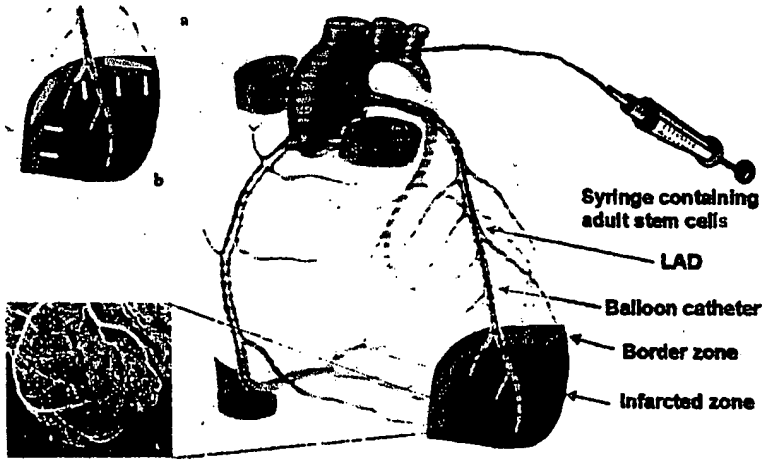

Figure 1. Procedure of cell transplantation into infarcted myocardium in humans. a, The balloon catheter enters the infarct-related artery and is placed above the border zone of the infarction. It is then inflated and the cell suspension is infused at high pressure under stop-flow conditions. b, In this way, cells are transplanted into the infarcted zone via the infarct-related vasculature (red dots). Cells infiltrate the infarcted zone. Blue and white arrows suggest the possible route of migration. c, A supply of blood flow exists within the infarcted zone.[35] The cells are therefore able to reach both the border and the infarcted zone.

into postinfarction tissue. A pilot study from our group demonstrated that intracoronary transplantation of autologous mononuclear BMCs 6 days after MI was associated with a marked decrease in infarct area and an increase in left ventricular (LV) function after 3 and 6 months of follow-up.[17] To confirm these results and validate this promising new therapy for MI, we established a clinical trial involving 20 patients for comparing the safety and bioefficacy of autologous BMC transplantation. All 20 patients underwent standard therapy, and 10 patients received additional intracoronary cell transplantation. All 20 patients were followed up for 3 months.

Methods

Patient Population

All 20 patients had suffered transmural infarction according to World Health Organization criteria with the involvement of the left anterior descending coronary artery (n=4), left circumflex coronary artery (n=3), or right coronary artery (n=13). Mean duration of infarct pain was 12±10 hours before invasive diagnostics and therapy. Patients had to be <70 years old and were excluded if one of the following criteria were met: screening >72 hours after infarction, cardiac shock, severe comorbidity, alcohol or drug dependency, or excessive travel distance to the study center.

After right and left heart catheterization, coronary angiography, and left ventriculography, mechanical treatment was initiated with recanalization of the infarct-related artery by balloon angioplasty (n=20) and subsequent stent implantation (n=19). All patients were monitored in our intensive care unit, and no arrhythmogenic events or hemodynamic impairments were recorded in either patient group.

All 20 patients were briefed in detail about the procedure of BMC transplantation. Informed consent was obtained from 10 patients, who formed the cell therapy group, whereas 10 patients who refused additional cell therapy served as controls. The local ethics committee of the Heinrich-Heine-University, Düsseldorf, approved the study protocol. All procedures conformed to institutional guidelines.

Before taking part in rehabilitation programs, all patients left the hospital with standard medication consisting of acetylsalicylic acid, an ACE inhibitor, a β-blocker, and a statin.

Bone Marrow Aspiration, Isolation, and Cultivation

Seven (±2) days after acute coronary angiography, bone marrow (~40 mL) was aspirated under local anesthesia from ilium of cell therapy patients (n=10). Mononuclear BMCs were isolated by Ficoll density separation on Lymphocyte Separation Medium (BioWhittaker) before the erythrocytes were lysed with H_2O. For overnight cultivation, 1×10^6 BMCs/mL were placed in Teflon bags (Vuelife, Cell Genix) and cultivated in X-Vivo 15 Medium (BioWhittaker) supplemented with 2% heat-inactivated autologous plasma. The next day, BMCs were harvested and washed 3 times with heparinized saline before final resuspension in heparinized saline. Viability was 93±3%. Heparinization and filtration (cell strainer, FALCON) was carried out to prevent cell clotting and microembolization during intracoronary transplantation. The mean number of mononuclear cells harvested after overnight culture was 2.8×10^7; this consisted of 0.65±0.4% AC133-positive cells and 2.1±0.28% CD34-positive cells. All microbiological tests of the clinically used cell preparations proved negative. As a viability and quality ex vivo control, 1×10^5 cells grown in H5100 medium (Stem Cell Technology) were found to be able to generate mesenchymal cells in culture.

Intracoronary Transplantation of BMCs

Five to nine days after onset of acute infarction, cells were directly transplanted into the infarcted zone (Figure 1). This was accomplished with the use of a balloon catheter, which was placed within the infarct-related artery. After exact positioning of the balloon at the site of the former infarct-vessel occlusion, percutaneous transluminal coronary angioplasty (PTCA) was performed 6 to 7 times for 2 to 4 minutes each. During this time, intracoronary cell transplantation via the balloon catheter was performed, using 6 to 7 fractional high-pressure infusions of 2 to 3 mL cell suspension, each of which contained 1.5 to 4×10^6 mononuclear cells. PTCA thoroughly prevented the backflow of cells and at the same time produced a stop-flow beyond the site of the balloon inflation to facilitate high-pressure infusion of cells into the infarcted zone. Thus, prolonged contact time for cellular migration was allowed.[18]

Functional Assessment of Hemodynamics

After 3 months, all 20 patients were followed up by left heart catheterization, left ventriculography, and coronary angiography. Ejection fraction, infarct region, and regional wall movement of the infarcted zone during ejection were determined by left ventriculography. Ejection fraction was measured with Quantcor software (Siemens). To quantify infarction wall movement velocity, 5 axes were placed perpendicular to the long axis in the main akinetic or dyskinetic segment of the ventricular wall. Relative systolic and diastolic lengths were measured, and the mean difference was divided by the systolic duration (in seconds). To quantify the infarct region, the centerline method according to Sheehan was used.[19] All hemodynamic investigations were obtained by two independent observers.

In the cell therapy group before and 3 months after cell transplantation, additional examinations for measuring hemodynamics and myocardial perfusion included dobutamine stress echocardiography, radionuclide ventriculography, catheterization of the right heart, and

TABLE 1. Baseline Characteristics of the Patients

Clinical Data	Cell Therapy	Standard Therapy	P
Characteristics			
No. of patients	10	10	...
Age, y	49±10	50±6	NS
Sex	Male	Male	...
Onset of infarction before angioplasty, h	10±8	13±11	NS
Coronary angiography			
No. of diseased vessels	1.7±0.9	2.1±0.7	NS
No. of patients with LAD/LCX/RCA as the affected vessel	4/1/5	0/2/8	...
No. of patients with stent implantation	9	10	...
Laboratory parameters			
Creatinine kinase, U/L	1138±1170	1308±1187	NS
Creatinine kinase-MB, U/L	106±72	124±92	NS
Bone marrow puncture after angioplasty, d	7±2	...	...
Mononuclear bone marrow cells, n ($\times 10^7$)	2.8±2.2	...	...

Values are mean±SD or number of patients.
NS indicates not significant; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; and RCA, right coronary artery.

stress-redistribution-reinjection ^{201}thallium scintigraphy. The contractility index P_{sys}/ESV was calculated by dividing LV systolic pressure (P_{sys}) by end-systolic volume (ESV). Perfusion defect was calculated by scintigraphic bull's-eye technique. Each examination was performed according to standard protocols.

There were no complications or side effects determined in any patient throughout the diagnostic or therapeutic procedure or within the 3-month follow-up period.

Statistical Analysis

All data are presented as mean±SD. Statistical significance was accepted when P was <0.05. Discrete variables were compared as rates, and comparisons were made by χ^2 analysis. Intra-individual comparison of baseline versus follow-up continuous variables was performed with a paired t test. Comparison of nonparametric data between the two groups was performed with Wilcoxon test and Mann-Whitney test. Statistical analysis was performed with SPSS for Windows (version 10.1).

Results

Clinical data between the two groups did not differ significantly. The range of creatinine kinase levels was slightly but not significantly higher in the standard therapy group than it was in the cell therapy group (Table 1).

Comparison of the 2 groups 3 months after cell or standard therapy showed several significant differences in LV dynamics, according to the global and regional analysis of left ventriculogram. The infarct region as a percentage of hypokinetic, akinetic, or dyskinetic segments of the circumference of the left ventricle decreased significantly in the cell therapy group (from 30±13 to 12±7%, $P=0.005$). It was also significantly smaller compared with the standard therapy group after 3 months ($P=0.04$). Within the standard therapy group, only a statistically nonsignificant decrease from 25±8 to 20±11% could be seen. Wall movement velocity over the infarct region rose significantly in the cell therapy group (from 2.0±1.1 to 4.0±2.6 cm/s, $P=0.028$) but not in the standard therapy group (from 1.8±1.3 to 2.3±1.6 cm/s, P=NS). No significant difference was observed between the two groups. Ejection fraction increased in both groups, albeit nonsignificantly (from 57±8 to 62±10% in the cell therapy group and from 60±7 to 64±7% in the standard therapy group) (Table 2).

Further significant improvement could also be seen on additional analysis of the cell therapy group alone. Perfusion defect was considerably decreased by 26% in the cell therapy group (from 174±99 to 128±71 cm², $P=0.016$, assessed by ^{201}thallium scintigraphy) (Figure 2). Parallel to the reduction in perfusion defect, improvement (Table 3) could also be seen in:

(1) Cardiac function, as revealed by increase in stroke volume index (from 49±7 to 56±7 mL/m², $P=0.010$) and ejection fraction (from 51±14 to 53±13%, P=NS).
(2) Cardiac geometry, as shown by decreases in both end-diastolic (from 158±20 to 143±30 mL, P=NS) and end-systolic volume (from 82±26 to 67±21 mL, $P=0.011$). Radionuclide ventriculography was used to acquire the data.
(3) Contractility as evaluated by an increase in the velocity of circumferential fiber shortening (from 20.5±4.2 to 24.4±7.7 mm/s, P=NS, assessed by stress echocardiography) and by a marked increase in the ratio of systolic pressure to end-systolic volume (from 1.81±1.44 to 2.27±1.72 mm Hg/mL, $P=0.005$).

Discussion

The present report describes the first clinical trial of intracoronary, autologous, mononuclear BMC transplantation for improving heart function and myocardial perfusion in patients after acute MI. The results demonstrate that transplanted autologous BMCs may lead to repair of infarcted tissue when applied during the immediate postinfarction period. These results also show that the intracoronary approach of BMC transplantation seems to represent a novel

TABLE 2. Comparison of Cell Therapy and Standard Therapy Groups

	Cell Therapy	Standard Therapy	P
No. of patients	10	10	...
Infarct region as functional defect			
Hypokinetic, akinetic, or dyskinetic region at 0 mo, %	30±13	25±8	NS
Hypokinetic, akinetic, or dyskinetic region at 3 mo, %	12±7	20±11	0.04
P	0.005	NS	...
Contractility indices			
Infarction wall movement velocity at 0 mo, cm/s	2.0±1.1	1.8±1.3	NS
Infarction wall movement velocity at 3 mo, cm/s	4.0±2.6	2.3±1.6	NS
P	0.028	NS	...
Hemodynamic data			
LV ejection fraction at 0 mo, %	57±8	60±7	NS
LV ejection fraction at 3 mo, %	62±10	64±7	NS
P	NS	NS	...

NS indicates not significant; 0 mo, zero months, which means the time of infarction; 3 mo, 3 months, which means the time of the follow-up examinations. All data were obtained according to analysis of left ventriculogram.

and effective therapeutic procedure for concentrating and/or depositing infused cells within the region of interest.

Neogenesis of both cardiomyocytes and coronary capillaries with some functional improvement has been shown recently by several investigators using bone marrow–derived cells in experimental infarction.[11–14,18,20–23] Moreover, transendothelial migration from the coronary capillaries and incorporation of cells into heart muscle has been observed experimentally.[3,12,24–26] Until now, clinical data only existed for the cell therapy of surgically treated chronic ischemic heart disease.[15,16] Our aim was to transform the encouraging results from animal models to a safe clinical setting. The most crucial questions we had to address while designing and realizing this trial were: (1) What cell population should we deliver? (2) Which application method is the most efficient? (3) When should the cells be transplanted?

In recent years, several laboratories have shown that environmentally dictated changes of fate (transdetermination) are not restricted to stem cells but may also involve progenitor cells at different steps of a given differentiation pathway (transdifferentiation). Moreover, mesenchymal stem cells may represent an ideal cell source for treating different diseases.[27] Adult, mononuclear BMCs contain such stem and progenitor cells (≤1%), eg, mesodermal progenitor cells, hematopoietic progenitor cells, and endothelial progenitor cells. In several animal infarction models it has been shown that: (1) Bone marrow hemangioblasts contribute to the formation of new vessels; (2) bone marrow hematopoietic stem cells differentiate into cardiomyocytes, endothelium,

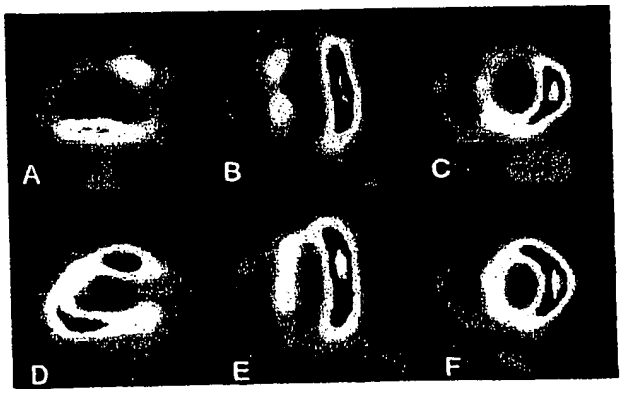

Figure 2. Improved myocardial perfusion of infarcted anterior wall 3 months after intracoronary cell transplantation subsequent to an acute anterior wall infarction detected by ^{201}thallium scintigraphy. The images on the left (A, D, sagittal) and in the middle (B, E) show the long axis, whereas those on the right (C, F, frontal) show the short axis of the heart. Initially the anterior wall, with green-colored apical and anterior regions, had reduced myocardial perfusion (A, B, C). Three months after cell transplantation the same anterior wall, now yellow in color, revealed a significant improvement in myocardial perfusion (D, E, F). All illustrations depict the exercise phase.

TABLE 3. Cardiac Function Analysis at 3-Month Follow-Up

	Before Cell Therapy	3 Months After Cell Therapy	P
No. of patients	10	10	...
Hemodynamic data			
LV ejection fraction, %	51±14	53±13	NS
Stroke volume index, mL/m^2	49±7	56±7	0.010
Cardiac geometry			
LV end-diastolic volume, mL	158±20	143±30	NS
LV end-systolic volume, mL	82±26	67±21	0.011
Contractility indices			
Circumferential fiber shortening, mm/s	20.5±4.2	24.4±7.7	NS
P_{sys}/ESV, mm Hg/mL	1.81±1.44	2.27±1.72	0.005
Infarct region as perfusion defect			
^{201}Thallium scintigraphy, cm^2	174±99	128±71	0.016

NS indicates not significant.

and smooth muscle cells[8-13]; (3) BMCs give rise to mesodermal progenitor cells that differentiate to endothelial cells[28]; and (4) endothelial progenitors can transdifferentiate into beating cardiomyocytes.[29] Thus, several different fractions of mononuclear BMCs may contribute to the regeneration of necrotic myocardium and vessels. In order to utilize this large and perhaps heterogeneous regenerative potential, we decided to use all mononuclear cells from the bone marrow aspirate as a whole, rather than a subpopulation. No further expansion was performed because experimental data have revealed a dramatic decline in the homing capacity of in vitro amplified hematopoietic stem or progenitor cells.[30]

The second question was how to deliver the cells most efficiently. When given intravenously, only a very small fraction of infused cells can reach the infarct region after the following injection: assuming a normal coronary blood flow of 80 mL/min per 100 g of LV weight, a quantity of 160 mL per left ventricle (assuming a regular LV mass of ≈200 g) will flow per minute.[31,32] This corresponds to only about 3% of cardiac output (assuming a cardiac output of 5000 mL/min).[31] Therefore, intravenous application would require many circulation passages to enable infused cells to come into contact with the infarct-related artery. Throughout this long circulation and recirculation time, homing of cells to other organs could considerably reduce the numbers of cells dedicated to cell repair in the infarcted zone. Thus, supplying the entire complement of cells by intracoronary administration obviously seems to be advantageous for the tissue repair of infarcted heart muscle and may also be superior to intraventricular injection,[33] because all cells are able to flow through the infarcted and peri-infarcted tissue during the immediate first passage. Accordingly, by this intracoronary procedure the infarct tissue and the peri-infarct zone can be enriched with the maximum available amount of cells at all times.

As stem cells differentiate into more mature types of progenitor cells, it is thought that a special microenvironment in so-called niches regulates cell activity by providing specific combinations of cytokines and by establishing direct cellular contact. For successful long-term engraftment, at least some stem cells have to reach their niches, a process referred to as homing. Mouse experiments have shown that significant numbers of BMCs appear in liver, spleen, and bone marrow after intravenous injection.[34] To offer the BMCs the best chance of finding their niche within the myocardium, a selective intracoronary delivery route was chosen. Presumably, therefore, fewer cells were lost by extraction toward organs of secondary interest by this first pass–like effect. To facilitate transendothelial passage and migration into the infarcted zone, cells were infused by high-pressure injection directly into the necrotic area, and the balloon was kept inflated for 2 to 3 minutes; the cells were not washed away immediately under these conditions.

The time point for delivery was chosen as 7 to 8 days after infarction onset for the following reasons:

(1) In dogs, infarcted territory becomes rich in capillaries and contains enlarged, pericyte-poor "mother vessels" and endothelial bridges 7 days after myocardial ischemia and reperfusion. Twenty-eight days later, a significant muscular vessel wall has already formed.[35] Thus, with such timing, cells may be able to reach the worst damaged parts and at the same time salvage tissue. Transendothelial cell migration may also be enhanced because an adequate muscular coat is not yet formed.

(2) Until now, only one animal study has attempted to determine the optimum time for cardiomyocyte transplantation to maximize myocardial function after LV injury. Adult rat hearts were cryoinjured and fetal rat cardiomyocytes were transplanted immediately, 2 weeks later, and 4 weeks later. The authors discussed the inflammatory process, which is strongest in the first days after infarction, as being responsible for the negative results after immediate cell transplantation, and they assumed that the best results seen after 2 weeks may have been due to transplantation before scar expansion.[36] Until now, however, no systematic experiments have been performed with BMCs to correlate the results of transplantation with the length of such a time delay.

(3) Another important variable is the inflammatory response in MI, which seems to be a superbly orchestrated interaction of cells, cytokines, growth factors and extracellular matrix proteins mediating myocardial repair. In the first 48 hours, debridement and formation of a fibrin-based provisional matrix predominates before a healing phase ensues.[37-40] Moreover, vascular endothelial growth factor is at its peak concentration 7 days after MI, and the decline of adhesion molecules (intercellular adhesion molecules, vascular cell adhesion molecules) does not take place before days 3 to 4 after MI. We assumed that transplantation of mononuclear BMCs within the "hot" phase of post-MI inflammation might lead them to take part in the inflammation cascade rather than the formation of functional myocardium and vessels.

Taking all of this into account, we can conclude that cell transplantation within the first 5 days after acute infarction is not possible for logistical reasons and is not advisable because of the inflammatory process. On the other hand, transplantation 2 weeks after infarction scar formation seems to reduce the benefit of cell transplantation. Although the ideal time point for transplantation remains to be defined, it is most likely between days 7 and 14 after the onset of MI, as in the present study.

This trial was designed as a phase I safety and feasibility trial, meaning that no control group is necessarily required. However, to validate the results, we correlated them with those obtained from 10 patients who refused to get additional cell therapy and thus received standard therapy alone. We are aware of the fact that such a comparison does not reach the power of a randomly allocated, blinded control group. However, the significant improvement with regard to infarct region, hemodynamics (stroke volume index), cardiac geometry (LV end-systolic volume), and contractility (P_{sys}/ESV and infarction wall movement velocity) did confirm a positive effect of the additional cell therapy because the changes observed in the standard therapy group failed to reach significance.

Another important factor for interpreting the results is time interval between onset of symptoms and revascularization of the infarct-related artery by angioplasty; this represents a crucial determinant of LV recovery. For patients with acute MI, it has

been shown that if the time interval is >4 hours, no significant changes in ejection fraction, regional wall motion, or ESV are observed after 6-month follow-up by echocardiography and angiography.[41] None of our 20 patients was treated by angioplasty within 4 hours after onset of symptoms. Our average time interval was 12±10 hours. Thus, PTCA-induced improvement of LV function can be nearly excluded; indeed, the only mild and nonsignificant changes within the standard therapy group are consistent with the above-mentioned data.[41] In contrast, the cell therapy group showed considerable and significant improvement in the same parameters, which may be attributed to BMC-mediated coronary angioneogenesis and cardiomyoneogenesis.

These results show that transplantation of autologous BMCs, as well as the intracoronary approach, represent a novel and effective therapeutic procedure for the repair of infarcted myocardium. For this method of therapy, no ethical problems exist, and no side effects were observed at any point of time. The therapeutic benefit for the patient's heart seems to prevail. However, further experimental studies, controlled prospective clinical trials, and variations of cell preparations are required to define the role of this new approach for the therapy of acute MI in humans.

References

1. Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction: experimental observations and clinical implications. *Circulation*. 1990;81:1161–1172.
2. Ertl G, Gaudron P, Hu K. Ventricular remodeling after myocardial infarction: experimental and clinical studies. *Basic Res Cardiol*. 1993;88:125–137.
3. Quaini F, Urbanek K, Beltrami AP, et al. Chimerism of the transplanted heart. *N Engl J Med*. 2002;346:5–15.
4. Leor J, Patterson M, Quinones MJ, et al. Transplantation of fetal myocardial tissue into infarcted myocardium of rat: a potential method for repair of infarcted myocardium? *Circulation*. 1996;94(suppl II):332–336.
5. Murry CE, Wiseman RW, Schwartz SM, et al. Skeletal myoblast transplantation for repair of myocardial necrosis. *J Clin Invest*. 1996;98:2512–2523.
6. Taylor DA, Atkins BZ, Hungspreugs P, et al. Regenerating functional myocardium: improved performance after skeletal myoblast transplantation. *Nat Med*. 1998;4:929–933.
7. Tomita S, Li RK, Weisel RD, et al. Autologous transplantation of bone marrow cells improves damaged heart function. *Circulation*. 1999;100(suppl II):247–256.
8. Blau HM, Brazelton TR, Weimann JM. The evolving concept of a stem cell: entity or function? *Cell*. 2001;105:829–841.
9. Krause DS, Theise ND, Collector MI, et al. Multi-organ, multi-lineage engraftment by a single bone marrow-derived stem cell. *Cell*. 2001;105:369–377.
10. Goodell MA, Jackson KA, Majka SM, et al. Stem cell plasticity in muscle and bone marrow. *Ann N Y Acad Sci*. 2001;938:208–218.
11. Orlic D, Kajstura J, Chimenti S, et al. Bone marrow cells regenerate infarcted myocardium. *Nature*. 2001;410:701–705.
12. Orlic D, Kajstura J, Chimenti S, et al. Mobilized bone marrow cells repair the infarcted heart, improving function and survival. *Proc Natl Acad Sci U S A*. 2001;98:10344–10349.
13. Kocher AA, Schuster MD, Szabolcs MJ, et al. Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function. *Nat Med*. 2001;7:430–436.
14. Tomita S, Mickle DA, Weisel RD, et al. Improved heart function with myogenesis and angiogenesis after autologous porcine bone marrow stromal cell transplantation. *J Thorac Cardiovasc Surg*. 2002;123:1132–1135.
15. Menasche P, Hagege AA, Scorsin M, et al. Myoblast transplantation for heart failure. *Lancet*. 2001;357:279–280.
16. Hamano K, Nishida M, Hirata K, et al. Local implantation of autologous bone marrow cells for therapeutic angiogenesis in patients with ischemic heart disease: clinical trial and preliminary results. *Jpn Circ J*. 2001;65:845–847.
17. Strauer BE, Brehm M, Zeus T, et al. Myocardial regeneration after intracoronary transplantation of human autologous stem cells following acute myocardial infarction. *Dtsch med Wschr*. 2001;126:932–938.
18. Wang JS, Shum-Tim D, Chedrawy E, et al. The coronary delivery of marrow stromal cells for myocardial regeneration: pathophysiologic and therapeutic implications. *J Thorac Cardiovasc Surg*. 2001;122:699–705.
19. Sheehan FH, Bolson EL; Dodge HT, et al. Advantages and applications of the Centerline method for characterizing regional ventricular function. *Circulation*. 1986;74:293–305.
20. Sussman M. Cardiovascular biology: hearts and bones. *Nature*. 2001;410:640–641.
21. Toma C, Pittenger MF, Cahill KS, et al. Human mesenchymal stem cells differentiate to a cardiomyocyte phenotype in the adult murine heart. *Circulation*. 2002;105:93–98.
22. Kamihata H, Matsubara H, Nishiue T, et al. Implantation of bone marrow mononuclear cells into ischemic myocardium enhances collateral perfusion and regional function via side supply of angioblasts, angiogenic ligands, and cytokines. *Circulation*. 2001;104:1046–1052.
23. Ferrari G, Cusella-De Angelis G, Coletta M, et al. Muscle regeneration by bone marrow-derived myogenic progenitors. *Science*. 1998;279:1528–1530.
24. Kawamoto A, Gwon HC, Iwaguro H, et al. Therapeutic potential of ex vivo expanded endothelial progenitor cells for myocardial ischemia. *Circulation*. 2001;103:634–637.
25. Robinson SW, Cho PW, Levitsky HI, et al. Arterial delivery of genetically labelled skeletal myoblasts to the murine heart: long-term survival and phenotypic modification of implanted myoblasts. *Cell Transplant*. 1996;5:77–91.
26. Bittner RE, Schofer C, Weipoltshammer K, et al. Recruitment of bone-marrow-derived cells by skeletal and cardiac muscle in adult dystrophic mdx mice. *Anat Embryol (Berl)*. 1999;199:391–396.
27. Jiang Y, Jahagirdar B, Reinhardt RL, et al. Pluripotency of mesenchymal stem cells derived from adult marrow. *Nature*. 2002;20:1–12.
28. Reyes M, Lund T, Lenvik T, et al. Purification and ex vivo expansion of postnatal human marrow mesodermal progenitor cells. *Blood*. 2001;98:2615–2625.
29. Condorelli G, Borello U, De Angelis L, et al. Cardiomyocytes induce endothelial cells to trans-differentiate into cardiac muscle: implications for myocardium regeneration. *Proc Natl Acad Sci U S A*. 2001;98:10733–10738.
30. Szilvassy SJ, Bass MJ, Van Zant G, et al. Organ-selective homing defines engraftment kinetics of murine hematopoietic stem cells and is compromised by ex vivo expansion. *Blood*. 1999;93:1557–1566.
31. Gregg DE, Fisher LC. Blood supply to the heart. In: *Handbook of Physiology*. Vol 2. Washington, DC: American Physiological Society; 1963:chap 44, 1517–1584.
32. Strauer BE. Myocardial oxygen consumption in chronic heart disease: role of wall stress, hypertrophy and coronary reserve. *Am J Cardiol*. 1979;4:730–740.
33. Toma C, Pittenger MF, Byrne BJ, et al. Adult human mesenchymal stem cells differentiate to a striated muscle phenotype following arterial delivery to the murine heart. *Circulation*. 2000;102(suppl II):II-683. Abstract.
34. Hendrikx PJ, Martens CM, Hagenbeek A, et al. Homing of fluorescently labeled murine hematopoietic stem cells. *Exp Hematol*. 1996;24:129–140.
35. Ren G, Michael LH, Entman ML, et al. Morphological characteristics of the microvasculature in healing myocardial infarcts. *J Histochem Cytochem*. 2002;50:71–79.
36. Li RK, Mickle DA, Weisel RD, et al. Optimal time for cardiomyocyte transplantation to maximize myocardial function after left ventricular injury. *Ann Thorac Surg*. 2001;72:1957–1963.
37. Frangogiannis NG, Smith CW, Entman ML. The inflammatory response in myocardial infarction. *Cardiovasc Res*. 2002;53:31–47.
38. Allgöwer M. *The Cellular Basis of Wound Repair*. Springfield, Ill: Charles C. Thomas; 1956.
39. Xie Y, Zhou T, Shen W, et al. Soluble cell adhesion molecules in patients with acute coronary syndrome. *Chin Med J*. 2000;113:286–288.
40. Soeki T, Tamura Y, Shinohara H, et al. Serial changes in serum VEGF and HGF in patients with acute myocardial infarction. *Cardiology*. 2000;93:168–174.
41. Sheiban I, Fragasso G, Rosano GMC, et al. Time course and determinants of left ventricular function recovery after primary angioplasty in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2001;38:464–471.